FENPROPATHRIN

RISK CHARACTERIZATION DOCUMENT

Volume I

HEALTH ASSESSMENT SECTION

MEDICAL TOXICOLOGY BRANCH, DEPARTMENT PESTICIDE REGULATION

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

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EXECUTIVE SUMMARY

INTRODUCTION

Prior to being sold or applied to crops in the state of California, pesticides must go through a comprehensive evaluation and registration process conducted by the California Environmental Protection Agency (Cal/EPA), Department of Pesticide Regulation (DPR). This process is also performed subsequent to federal registration by the United States Environmental Protection Agency (U.S. EPA). The Medical Toxicology Branch of DPR is responsible for reviewing the toxicology data base for all new and existing pesticides. These reviews consider the adequacy of the tests and the potential for adverse health effects in humans. Following an analysis of worker exposure (estimated by the Worker Health and Safety Branch of DPR) the Medical Toxicology Branch evaluates the pesticide's overall risk potential and generates a risk characterization document (RCD).

This document characterizes the potential risk associated with occupational and dietary exposures to the pesticide fenpropathrin. Fenpropathrin is the active ingredient of Danitol® and Tame®, products under consideration for registration in the state of California. Fenpropathrin is the common name for (RS)-α-cyano-3-phenoxybenzyl-2,2,3,3-tetramethyl-cyclopropane-carboxylate. This compound is a synthetic pyrethroid with insecticidal/acaricidal properties. Fenpropathrin is marketed in the United States by the Valent Corporation on behalf of the Sumitomo Chemical Company. Fenpropathrin is relatively unstable under normal environmental conditions. The active ingredient and its metabolites are immobile in most soils, and consequently are not expected to have a high potential for leaching. Furthermore, fenpropathrin and its metabolites are rapidly degraded under normal environmental conditions. Animal metabolism studies indicate that this pesticide is rapidly excreted in the urine and feces, i.e., approximately 90% of the material is excreted within the first 48 hours after exposure.

Both of the products currently under review are emulsifiable concentrates with 30.9 % fenpropathrin. The Danitol® product is intended for use on cotton for the control of a number of pests including sweet potato whiteflies. Tame® is intended for use on non-food greenhouse crops (i.e., various plants, shrubs, and trees) for the control of whiteflies, mites and other pests.

RISK ASSESSMENT PROCESS

The risk assessment process incorporates four aspects: hazard identification, dose-response evaluation, exposure assessment, and risk characterization.

Hazard identification entails review and evaluation of the toxicological properties of each pesticide. The dose-response assessment then considers the toxicological properties and estimates the amount that could potentially cause an adverse effect. The amount that will not result in an observable or measurable effect is the No-Observed-Effect Level (NOEL). A basic premise of toxicology is that at a high enough dose, virtually all substances will cause toxic manifestations. Chemicals are often referred to as "dangerous" or "safe", as though these concepts were absolutes. In reality, these terms describe chemicals that require low or high dosages, respectively, to cause toxic effects. Toxicological activity is determined in a battery of experiential studies that define the types of toxic effects that can be caused, and the exposure levels (doses) at which effects may be seen. State and federal testing requirements mandate that substances be tested in laboratory animals at doses high enough to produce toxic effects, even if such testing involves chemical levels many times higher than those to which people might be exposed.

In addition to the intrinsic toxicological activity of the pesticide, the other parameters critical to determining risk potential are the level, frequency and duration of exposure. The purpose of the exposure evaluation is to determine the potential amount of the pesticide likely to be delivered through occupational, or dietary routes on an acute or chronic basis.

The risk characterization then integrates the toxic effects observed in the laboratory studies, conducted with high dosages of pesticide, to potential human exposures to low dosages of pesticides in the diet or work place. The potential for possible non-oncogenic adverse health effects in human populations is generally expressed as the margin of safety, which is the ratio of the dosage that produced no effects in laboratory studies to the estimated dietary and work related dosage. For oncogenic effects, the probability of risk is calculated as the product of the cancer potency of the pesticide and the estimated human dosage.

TOXICOLOGY

Experimental studies with this pesticide have demonstrated toxic activity in laboratory animals. While a comprehensive toxicology battery has been completed with fenpropathrin, the adverse responses appear to be restricted to acute effects, primarily related to neurotoxicity. No clear indication of chronic toxicity, oncogenicity, or developmental toxicity were detected. Studies indicate that this pesticide may have mutagenic potential in bacteria and in mammalian cells grown *in vitro*.

EXPOSURE ANALYSIS

For Danitol® both occupational and dietary exposure were evaluated. For occupational exposure, the dermal route was assumed to be the only route of significance. For Tame®, occupational and dietary exposures were considered with occupational exposure including inhalation exposure. Dietary exposure was considered for cotton and tomato byproducts. The inclusion of tomatoes was based on a current Section 18 registration (exemption from registration requirements) for the use of Danitol® on tomatoes in California.

In estimating dietary exposure to fenpropathrin, residue data were obtained from registrant supplied field trials for cotton and tomatoes. Since there is potential for fenpropathrin residues to be present in the feed of various domestic farm animals, meats, poultry, and dairy products they were also considered. The residues used for food products from animals were extrapolated either from field study data or tolerance levels.

RISK EVALUATION

On the basis of the indicated effects and estimated dosages, margins of safety were calculated for occupational and dietary exposures.

No clear indication of chronic toxicity or oncogenicity has been demonstrated for fenpropathrin. Furthermore, on the basis of the current toxicology data base, estimated daily averages for chronic exposures would be significantly less than predicted for acute and short-term exposures. Determination of dosages and margins of safety for chronic exposure were not, therefore, conducted. It is assumed that the use of fenpropathrin that results in exposure levels with acceptable margins of safety for acute and short-term human exposure will be adequate for any potential chronic exposure protection.

Based on the current data base, all margins of safety for acute occupational and dietary exposure to fenpropathrin from Danitol® (proposed for use on cotton), and Tame® (proposed for use on greenhouse crops), are greater than 500. Margins of safety for average short-term exposure to fenpropathrin for workers using Danitol® ranged from 140 to 2,500. The margin of safety for cotton scouts was 140. For all other occupations the margins of safety were greater than 600. Margins of safety for maximum short-term exposure to fenpropathrin for workers using Danitol® ranged from 61 to 1,200, with cotton scouts having the margin of safety of 61. Margins of safety for average short-term exposure to fenpropathrin for workers using Tame® were 120, 270, and 1600 for harvesters, applicators, and mixer/loaders, respectively. Margins of safety for maximum short-term exposure to fenpropathrin for workers using Tame® were 73, 110, and 1200 for harvesters, applicators, and mixer/loaders, respectively. Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures may be an unrealistic estimation. The values for harvesters involved with the use of Tame® assumes a label modification to require the use of gauntlet gloves. Without this requirement, exposure would be significantly increased for this occupational activity.

CONCLUSIONS

The toxicology data base for fenpropathrin has indicated potential adverse effects in animal studies. These effects are generally associated with neurotoxicity and appear to be primarily a response to acute exposure. No clear indication of chronic toxicity, oncogenicity, or developmental toxicity was demonstrated. Studies did indicate that this pesticide may have mutagenic potential in bacteria and in mammalian cells grown *in vitro*. Based on the current data base, all margins of safety for acute occupational and dietary exposure to fenpropathrin from Danitol® (proposed for use on cotton), and Tame® (proposed for use on greenhouse crops), are greater than 100. For short-term exposures, all margins of safety greater than 100 except those for cotton scouts and greenhouse harvesters when estimates were based on maximum potential exposure (*the values for harvesters involved with the use of Tame® assumed a label modification that requires the use of gauntlet gloves. Without this modification, exposure would be significantly increased for this occupation*). Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures, may be an unrealistic estimate. In general, a margin of safety equal to or greater than 100 is considered adequate for the protection of human health when it is based on NOELs from non-human mammalian studies. When the potential toxicity is considered severe (e.g., tremors and death), a larger margin of safety may be warranted.

An additional dietary assessment of acute risk potential, based on residue levels set at U.S. EPA tolerances, indicated that little potential exists for adverse health effects from dietary exposure to fenpropathrin.

CONTRIBUTORS AND ACKNOWLEDGMENTS

Author:	Joseph P. Frank, D.Sc., Staff Toxicologist Health Assessment Section, Medical Toxicology Branch
Toxicology Reviews:	Joyce Gee, Ph.D., Senior Toxicologist SB-950 Data Review Section, Medical Toxicology Branch
	Peter Leung, Ph.D., Staff Toxicologist SB-950 Data Review Section, Medical Toxicology Branch
Dietary Exposure:	Wesley C. Carr, Jr., M.S., Associate Pesticide Review Scientist Health Assessment Section, Medical Toxicology Branch
Environmental Fate:	Michael L. Papathakis, B.S., Senior Pesticide Evaluation Scientist Pesticide Registration Branch
	Carolyn J. Rech, B.S., Associate Pesticide Review Scientist Health Assessment Section, Medical Toxicology Branch
Peer Review:	Keith F. Pfeifer, Ph.D., D.A.B.T., Senior Toxicologist Health Assessment Section, Medical Toxicology Branch
	Jay P. Schreider, Ph.D., Primary State Toxicologist Medical Toxicology Branch
	Lori O. Lim, Ph.D., D.A.B.T., Staff Toxicologist Health Assessment Section, Medical Toxicology Branch

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I. SUMMARY

A. INTRODUCTION

This document characterizes the potential risk associated with dietary and occupational exposures to the pesticide fenpropathrin. Fenpropathrin is the active ingredient of Danitol® and Tame®, products under consideration for registration in the state of California. This assessment was performed under the provisions of the California Birth Defect Prevention Act (Senate Bill 950), and the Assembly Bill 2161 (sometimes referred to as the Food and Safety Act). Senate Bill 950 requires a scientific determination that use of a registered pesticide will not cause significant adverse health effects. Assembly Bill 2161 requires risk assessments on the dietary exposure to pesticides in both raw and processed foods.

Fenpropathrin is the common name for (RS)-α-cyano-3-phenoxybenzyl-2,2,3,3-tetramethyl-cyclopropane-carboxylate. This compound is a synthetic pyrethroid with insecticidal/acaricidal properties. Fenpropathrin is marketed in the United States by the Valent Corporation on behalf of the Sumitomo Chemical Company. The products currently under review in California, Danitol® 2.4 EC and Tame® 2.4 EC, are emulsifiable concentrates with 30.9 % fenpropathrin. The Danitol® product is intended for use on cotton to control a number of pests including sweet potato whiteflies. Tame® is intended for use on non-food greenhouse crops (i.e., various plants, shrubs, and trees) for the control of whiteflies, mites and other pests.

B. TOXICOLOGY

Experimental studies with this pesticide have demonstrated toxic activity in laboratory animals, primarily related to neurotoxicity. While a comprehensive toxicology battery has been completed with fenpropathrin, the adverse responses appear to be restricted to acute effects. Reported clinical signs have included: muscular fibrillation, diarrhea, tremors, ataxia, decreased spontaneous activity, limb paralysis, irregular respiration, salivation, urinary incontinence, loss of righting reflex, hyperpnea, dyspnea, hyperexcitability, convulsions, lacrimation, nasal discharge, erythema, edema and death. There was no clear indication of chronic toxicity, oncogenicity, or developmental toxicity. Studies indicate that this pesticide may have mutagenic potential in bacteria and in mammalian cells grown *in vitro*.

Acute NOELs for fenpropathrin have been selected for both the oral and dermal routes of exposure for this risk assessment. The acute oral NOEL of 6 mg/kg was derived from a rat developmental study (Morseth, 1990). Death, convulsions, ataxia and tremors occurred in this study between days one and seven in rats treated with 10 mg/kg/day. The acute dermal NOEL of 100 mg/kg was derived from acute dermal LD_{50} studies conducted in rats and mice (Kohda, 1979; and Kohda and Kadota, 1980c, respectively). In both studies, the NOELs were based on ataxia, tremors and hypersensitivity.

Clinical signs have also been reported in animals following short-term exposures to fenpropathrin (where short-term exposure is defined as multiple exposure for a period of 1 to 3 weeks). In a chronic feeding study, female dogs administered 7.7 mg/kg/day fenpropathrin exhibited tremors, ataxia, and languidity within two weeks of initial dosing (Pence *et al.*,1984). The NOEL established from this study was 3 mg/kg/day. This NOEL for short-term exposure was supported by clinical signs observed in the second week of a reproductive study conducted with rats. In that study a NOEL of 3.1 mg/kg/day was established based on tremors and deaths observed at 9.1 mg/kg/day.

C. EXPOSURE

For Danitol® both occupational and dietary exposure were considered. For occupational exposure, the dermal route was assumed to be the only route of significance. For Tame®, occupational and dietary exposures were considered with occupational exposure including inhalation exposure. Dietary exposure was considered for cotton and tomato byproducts. The inclusion of tomatoes was based on a current Section 18 registration (exemption from registration requirements) for the use of Danitol® on tomatoes in California.

In estimating dietary exposure to fenpropathrin, residue data were obtained from registrant supplied field trials for cotton and tomatoes. Since there is potential for fenpropathrin residues to be present in the feed of various domestic farm animals, meats, poultry, and dairy products of these commodities were considered in the assessment of exposure. The residues used for food products from animals was extrapolated either from field study data or tolerance levels.

For workers using Danitol®, estimated average acute dosages of fenpropathrin ranged from approximately 1 μg/kg body weight to 25 μg/kg body weight. These values included both occupational and dietary exposures. The dietary contribution was approximately 0.5 μg/kg body weight and was based on the 95th percentile exposure estimate to the general population age 16 and above. The maximum predicted dosages ranged from approximately 3 μg/kg body weight to 58 μg/kg body weight. For both average and maximum exposure scenarios, the occupation with the highest exposure estimates was cotton scouts. For short-term exposures, i.e., 1 to 3 weeks, the estimated average dosages of fenpropathrin ranged from approximately 1 μg/kg body weight to 21 μg/kg body weight. Maximum potential exposure estimates ranged from 2 to 49 μg/kg body weight.

With Tame®, estimated average fenpropathrin acute dosages were approximately 1, 11, and 30 μg/kg body weight for mixer/loaders, applicators, and harvesters, respectively. The maximum predicted dosages were approximately 2, 32, and 45 μg/kg body weight for mixer/loaders, applicators, and harvesters, respectively. As with occupational exposure to Danitol®, the dietary contribution was approximately 0.5 μg/kg body weight and was based on the 95th percentile exposure estimate to the general population age 16 and above. For short-term exposures, estimated average fenpropathrin dosages were approximately 2, 11, and 26 μg/kg body weight for mixer/loaders, applicators, and harvesters, respectively. The maximum predicted dosages were approximately 2, 28, and 41 μg/kg body weight for mixer/loaders, applicators, and harvesters, respectively.

For nonoccupational exposure to fenpropathrin, the potential acute dietary dosage of fenpropathrin from cotton and tomato products ranged from approximately 0.4 to 1.3 μg/kg body weight/day The population subgroup with the highest potential dosage was children ages 1 to 6. Estimated dosages were based on the 95th percentile of consumer-day exposures.

D. RISK CHARACTERIZATION

On the basis of the indicated effects and estimated dosages, margins of safety were calculated for both occupational and dietary exposures to fenpropathrin.

No clear indication of chronic toxicity or carcinogenicity has been demonstrated for fenpropathrin. Furthermore, on the basis of the current toxicology data base, estimated daily averages for chronic exposures would be significantly less than predicted for acute and short-term exposures. Determination of dosages and margins of safety for chronic exposure were not, therefore, conducted. It is assumed that the use of fenpropathrin that results in exposure levels with acceptable margins of safety for acute and short-term human exposure will be adequate for any potential chronic exposure protection.

Based on the current data base, all margins of safety for acute occupational and dietary exposure to fenpropathrin from Danitol® (proposed for use on cotton), and Tame® (proposed for use on greenhouse crops), are greater than 500. Margins of safety for average short-term exposure to fenpropathrin for workers using Danitol® ranged from 140 to 2,500. The margin of safety for cotton scouts was 140. For all other occupations the margins of safety were greater than 600. Margins of safety for maximum short-term exposure to fenpropathrin for workers using Danitol® ranged from 61 to 1,200, with cotton scouts having the margin of safety of 61. Margins of safety for average short-term exposure to fenpropathrin for workers using Tame® were 120, 270, and 1600 for harvesters, applicators, and mixer/loaders, respectively. Margins of safety for maximum short-term exposure to fenpropathrin for workers using Tame® were 73, 110, and 1200 for harvesters, applicators, and mixer/loaders, respectively. Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures, may be an unrealistic estimation. The values for harvesters involved with the use of Tame® assumes a label modification to require the use of gauntlet gloves. Without this requirement, exposure would be significantly increased for this occupational activity.

E. CONCLUSIONS

The toxicology data base for fenpropathrin has indicated potential adverse effects in animal studies. These effects are generally associated with neurotoxicity and appear to be primarily a response to acute exposure. No clear indication of chronic toxicity, oncogenicity, or developmental toxicity was demonstrated. Studies did indicate that this pesticide may have mutagenic potential in bacteria and in mammalian cells grown *in vitro*. Based on the current data base, all margins of safety for acute occupational and dietary exposure to fenpropathrin from Danitol® (proposed for use on cotton), and Tame® (proposed for use on greenhouse crops), are greater than 100. For short-term exposures, all margins of safety greater than 100 except those for cotton scouts and greenhouse harvesters when estimates were based on maximum potential exposure (*the values for harvesters involved with the use of Tame® assumed a label modification that requires the use of gauntlet gloves. Without this modification, exposure would be significantly increased for this occupation*). Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures, may be an unrealistic estimate. In general, a margin of safety equal to or greater than 100 is considered adequate for the protection of human health when it is based on NOELs from non-human mammalian studies. When the potential toxicity is considered severe (e.g., tremors and death), a larger margin of safety may be warranted.

An additional dietary assessment of acute risk potential, based on residue levels set at U.S. EPA tolerances, indicated that little potential exists for adverse health effects from dietary exposure to fenpropathrin.

II. INTRODUCTION

This document characterizes the potential risk associated with occupational and dietary exposures to the pesticide fenpropathrin. Fenpropathrin is the active ingredient of Danitol® and Tame®, products under consideration for a Section 3 (full) registration in the state of California. This assessment was performed under the provisions of the California Birth Defect Prevention Act (Senate Bill 950), and Assembly Bill 2161 (sometimes referred to as the Food and Safety Act). Senate Bill 950 requires a scientific determination that use of a registered pesticide will not cause significant adverse health effects. Assembly Bill 2161 requires risk assessments on the dietary exposure to pesticides in both raw agricultural commodities and processed foods. The toxicology data base submitted to the California Environmental Protection Agency (Cal/EPA), Department of Pesticide Regulation (DPR), has identified possible adverse effects. These effects were established in chronic toxicity, reproduction, developmental, and neurotoxicity studies. Furthermore, this pesticide is potentially genotoxic in bacteria and in mammalian cells grown *in vitro*.

A. CHEMICAL IDENTIFICATION

Fenpropathrin is the common name for (RS)-α-cyano-3-phenoxybenzyl-2,2,3,3-tetramethyl-cyclopropane-carboxylate. Fenpropathrin is a synthetic pyrethroid with insecticidal/acaricidal properties. Pyrethroids are generally divided into two classes based on their effects on the cercal sensory nerves *in vitro* and *in vivo* and on the symptomology they produce in dosed cockroaches (Gammon, 1985). Type I pyrethroids act to induce repetitive firing in a cercal sensory nerve. The poisoning symptoms of Type I compounds include restlessness, incoordination, hyperactivity, prostration, and paralysis. Type II pyrethroids are generally α-cyanophenoxybenzyl pyrethroids. They do not induce repetitive firing and are associated with a different set of symptoms, including a pronounced convulsive phase. Fenpropathrin is an unique compound in that it appears to have both Type I and Type II properties. It produces repetitive firing but is associated with Type II symptoms. Fenpropathrin is marketed in the United States by the Valent Corporation on behalf of the Sumitomo Chemical Company. The products currently under review in California, Danitol®, 2.4 EC and Tame® 2.4 EC, are emulsifiable concentrates with 30.9 % fenpropathrin. The Danitol® product is intended for use on cotton to control a number of pests including sweet potato whiteflies. Tame® is intended for use on non-food greenhouse crops (i.e., various plants, shrubs, and trees) for the control of whiteflies, mites and other pests.

B. REGULATORY HISTORY

Technical grade fenpropathrin was registered with the U.S. Environmental Protection Agency in December, 1989. The registration is for non-food greenhouse use only. Experimental Use Permits (EUP) were approved by the California Department of Food and Agriculture for use on cotton and grapes in 1986. In response to a Section 18 (exemption from registration requirements) petition by the Imperial County Whitefly Management Committee (El Centro, California), DPR conducted a risk assessment for the use of Danitol® on tomatoes (Frank and Carr, 1992). That risk assessment indicated that an adequate margin of safety did not exist for mixer/loaders using an open pour system during aerial application.

C. TECHNICAL AND PRODUCT FORMULATIONS

In the state of California, Danitol® 2.4 EC is currently registered under a Section 18 for use on tomatoes for the control of whiteflies. No fenpropathrin products currently hold a Section 3 registration (full registration) in California. The two products under consideration are Danitol® 2.4 EC and Tame® 2.4 EC. Both products are emulsifiable concentrates with 30.9 % fenpropathrin. Each gallon of liquid formulation contains 2.4 lb of fenpropathrin.

For use on cotton, the proposed label specifies that a maximum of 0.3 lb active ingredient (a.i.) be applied per acre. In any single season, no more than 0.8 lb a.i. (equivalent to 3 applications) can be applied per acre per season. The preharvest interval is 21 days, however, there is no specification for the minimum interval between successive applications, other than the requirement that worker entry into a treated area is prohibited for 24 hours after treatment. Protective clothing required by the label for applicators and "other handlers" include: long sleeved shirts, long pants, socks, shoes, chemical resistant gloves, and protective eyeware.

For use on greenhouse crops, the label specifies that a maximum concentration of 0.3 lb a.i. diluted in 100 gallons of water be used for each application, for a maximum of 3 successive applications. No requirement for the minimum interval between successive applications is indicated. Reentry to treated areas is allowed as soon as the spray has dried.

D. USAGE

Fenpropathrin has been used in connection with Experimental Use Permits and a Section 18 registration. It has been estimated that 46.9 lb of fenpropathrin were used on tomatoes in California in 1993. The total number of treated acreage in 1993 was 252.

E. ILLNESS REPORTS

No occupational illnesses have been reported in California.

F. PHYSICAL AND CHEMICAL PROPERTIES

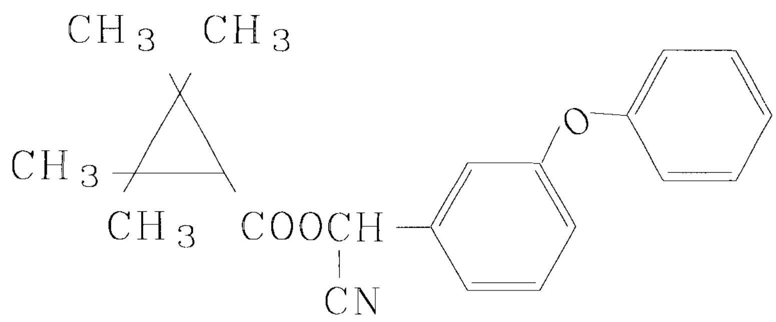
Chemical Name:
(RS)-α-cyano-3-phenoxybenzyl-2,2,3,3-tetramethyl-cyclopropane-carboxylate

Common Name:
fenpropathrin

Other Names:
Danimen®, Danitol®, Herald®, Meothrin®, Rody®, Tame®, SD-41706, S-3206, WL-41706, XE-938

Chemical Family:
Pyrethroid

Structural Formula:



Empirical Formula:
$C_{22}H_{22}NO_3$

Molecular Weight:
349

Melting Point:
45 - 50°C

Boiling Point:
377°C

Water Solubility:
0.33 mg/L at 25°C

Vapor Pressure:
5.50×10^{-6} mmHg at 20°C
9.74×10^{-6} mmHg at 25°C

Octanol/Water Partition Coefficient:

1×10^{6}

G. ENVIRONMENTAL FATE

Summary

Fenpropathrin is relatively unstable under environmental conditions encountered in the field. The active ingredient and metabolites are immobile in most soils, and consequently, have a low potential to leach. Although these compounds remain at the application site, they will not accumulate following multiple applications and are not taken up by rotational crops. Fenpropathrin is degraded primarily by microbial metabolism and chemical reactivity. Sunlight contributes to degradation both directly by photolysis of parent compound and metabolites, and indirectly as an accelerator of other chemical processes.

1. Hydrolysis/Photolysis

Fenpropathrin was examined for hydrolysis in water at pH 5, 7, and 9. The compound was stable at pH 5 and pH 7 ($t½$ = 295 to 607 days), but was hydrolyzed at a moderate rate at pH 9 ($t½$ = 14-17 days)(Concha *et al.*, 1992a; Papathakis, 1993). Takahashi *et al.* (1985a) studied the hydrolysis of fenpropathrin in several different aqueous media, including river and sea water. Fenpropathrin was fairly stable under neutral and acidic conditions with half-lives ranging from 38 to 1,280 days. Under basic conditions and/or elevated temperatures (pH 9 over 25 C, and pH 8 over 55 C) fenpropathrin was unstable with half-lives of less than 3 days.

Predominant hydrolysis reactions were cleavage of the ester linkage and hydration of the cyano group. Major hydrolysis products were the amide analog of fenpropathrin ($CONH_2$-fenpropathrin), tetramethyl-1-cyclopropane carboxylic acid (TMPA), TMPA-carboxamide, and 3-phenoxybenzoic acid (3-PBA).

2. Aqueous Photolysis

Aqueous photolysis of fenpropathrin was examined under natural sunlight conditions for a 30 day period. Although there were some discrepancies between the pilot and definitive studies, these data indicate that sunlight may accelerate the degradation of fenpropathrin in aqueous solutions (Jalai-Araghi, *et al.* 1992; Papathakis, 1993).

The degradation of fenpropathrin exposed to natural sunlight was also examined in distilled water, natural waters (river and sea water, pH 8), aqueous humic acid (pH 6.3) and 2% acetone solutions (Takahashi *et al.*, 1985b). Fenpropathrin was stable in distilled water with a half-life of more than 6 weeks. Photolysis occurred at various rates in all other aqueous media. Half-lives were 0.5, 11,19, and 42 days for acetone solution, sea water, river water, and humic acid solution, respectively. Photo-reactions were apparently enhanced by natural substances in water that may act as photosensitizers.

Predominant aqueous photolysis reactions were hydration at the cyano group and ester bond cleavage followed by photomineralization of the cyano fragment to carbon dioxide. The major photodegradates were $CONH_2$-fenpropathrin, the decarboxylate derivative, ester cleavage products, and carbon dioxide.

3. Soil Photolysis

The reaction kinetics of fenpropathrin photolysis on soil surfaces and the resulting degradation products were studied by several investigators (Dureja, 1990; Concha *et* *al.*, 1992b; Takahashi *et al.*, 1985b, and Katagi, 1993). Fenpropathrin was primarily degraded via chemical reactions that were accelerated by the presence of sunlight. Chemical reactivity was primarily a function of soil moisture content and soil characteristics. The influence of photolysis was a function of light intensity.

Fenpropathrin photolysis on sandy loam soil was examined under tropical sunlight and ultraviolet light conditions, and found to readily degrade (Dureja, 1990). Fenpropathrin was applied at the rate of 1.3 $\mu g/cm^2$ to soil samples and exposed to sunlight for 15 days. Only 12% remained as parent compound after the study period ($t\frac{1}{2}$ =3-4 days).

Concha *et al.* (1992b) found that no significant degradation occurred when fenpropathrin was applied to thin-layer plates (TLP) of sandy loam soil and exposed to natural sunlight for 30 days. In contrast, Takahasi *et al.* (1985b) found that photodegradation of fenpropathrin on TLP's was significant. Fenpropathrin was applied to light clay, sandy clay loam, and sandy loam soils (0.6% to 10.9% moisture), then exposed to natural sunlight for 14 days. Photodegradation was rapid with half-lives ranging from 3.3 to 10.4 days (Papathakis, 1993).

The findings of a study by Katagi (1993) may help to explain the differences in pathways and rates of soil photolysis observed in the previously cited studies. The effect of soil moisture content and UV irradiation on the degradation of fenpropathrin was examined on TLP's of clay loam and two loam soils. Soil moisture was adjusted to levels ranging from 0% (oven-dried) to 100%, fortified with fenpropathrin, and continuously irradiated with artificial light for the equivalent of 14 days. The degradation profile of fenpropathrin changed significantly with soil moisture content. Degradation pathways and rates were also influenced by soil characteristics such as clay quantity and species, and organic matter. A constant degradation rate was observed in soils with moisture content exceeding 30%. Degradation rates increased significantly in soils with moisture content below 17%. In soils with 0% moisture, 90% of the ^{14}C-fenpropathrin degraded within the first three days. Acid-catalyzed reactions, such as hydration of the cyano group followed by hydrolysis of the amide group, were predominant in soils with low moisture content (<50%). With an increase in soil moisture there was a decrease in soil acidity; thus, a retardation in the acid-catalyzed reactions. The predominant reactions in soils with a high moisture content (50%) were cleavage of the ester linkage and hydroxylation. Degradation reactions observed in high moisture soils were similar to those observed during anaerobic and aerobic soil metabolism, although the rates were significantly less. Primary degradation products for both types of reactions were $CONH_2$-fenpropathrin, COOH-fenpropathrin, phenoxybenzoic acid, and carbon dioxide. In conclusion, clay surface acidity as a function of soil type and moisture, rather than photolysis, was the primary factor influencing the degradation of fenpropathrin. Photolysis was a secondary degradation pathway and was also found to accelerate other degradation reactions.

4. Soil Metabolism

Fenpropathrin is metabolized in soil via cleavage of the ester or diphenyl ether bonds, hydroxylation, and hydrolysis of the cyano group to $CONH_2$ and COOH groups (Mikami *et al.*, 1983). Degradation products were desphenyl-fenpropathrin, 4'-OH-fenpropathrin, phenoxybenzoic acid, and CONH2-fenpropathrin which was further degraded to COOH-fenpropathrin. Major terminal products of aerobic metabolism were carbon dioxide and non-extractable residues. Fenpropathrin degradation in soil appears to be mediated, in part, by both aerobic and anaerobic microorganisms.

The anaerobic metabolism of fenpropathrin was examined in loam soil (Daly and Williams, 1990; Papathakis, 1993). Treated soil was aged under aerobic conditions for one month, followed by 61 days under anaerobic conditions. The half-life of fenpropathrin under anaerobic conditions was 186 days.

Mikami *et al.* (1983) studied the degradation of fenpropathrin in light clay and sandy clay loam soils under aerobic, anaerobic, and sterile conditions. Fenpropathrin degraded rapidly under aerobic conditions with only 2.5% to 4% of the parent compound remaining after 24 weeks (t½ = 41-46 days) (Papathakis, 1993). Fenpropathrin was degraded at a slower rate under anaerobic conditions with 85% to 87% of the parent compound remaining after 8 weeks. No appreciable degradation occurred in the sterile soils. Non-extractable residues reached a maximum of 50% in aerobic soils, but never exceeded 10% in the anaerobic and sterilized soils.

Aerobic metabolism of fenpropathrin in a silt loam soil was studied over a one year period (Cranor, 1989). The major products detected after the study period were the parent compound (18%), carbon dioxide (60%) and non-extractable residues (18%). Using a first-order model, the half-life of fenpropathrin was 152 days.

5. Soil Mobility

The leaching behavior of ^{14}C-fenpropathrin was examined in light clay, sandy clay loam, clay loam, and sand soils (Sakata *et al.*, 1990). Treated soils were either used immediately or aged for 4 weeks under dark, aerobic conditions. Under both aged and non-aged conditions, little radioactivity (^{14}C) was detected in the elute from the light clay, sandy clay loam, and clay loam soils. In comparison, 21-43% of the applied ^{14}C was detected in the elute from sand soil. Both parent compound and degradation products were detected in elute and soils. In conclusion, fenpropathrin does not readily leach and is considered relatively immobile in soil.

The adsorption and desorption properties of fenpropathrin was examined in sandy loam, silt loam, clay loam and loam soils, and aquatic sediments. The compound was found to adsorb to all soils and sediment. Data indicate that fenpropathrin is relatively immobile and is not expected to leach through soil (Lee, 1992; Papathakis, 1993).

6. Field Accumulation and Dissipation

The accumulation and dissipation of fenpropathrin was examined under various field conditions. Data demonstrate that fenpropathrin does not build up in soils following multiple applications, degrades at a moderate to fast rate, is not likely to leach under field conditions, and will not contaminate rotational crops.

Four applications of fenpropathrin to a California vineyard and bare ground at rate of 0.2 - 0.4 lbs ai/acre were performed at 10-14 day intervals (Fujie, 1990a; Fujie, 1991). Soil core samples were collected during, and for an extended period following applications. Maximum levels of fenpropathrin and $CONH_2$-fenpropathrin were detected shortly after the last application. Residues dissipated rapidly, with half-lives of the parent compound and metabolite ranging from 10-14 days. Residues were confined to the top 15 cm of soil although test plots were irrigated, indicating that there was no vertical movement of the compound.

Multiple applications to an orchard and cotton field at the rate of 0.4 lbs ai/acre were performed at 14-22 day intervals (Papathakis, 1993). Soil core samples were collected during and up to 538 days following the last application. Fenpropathrin dissipated rapidly, with a half-life of 8 days from the orchard site and 40 days from the cotton field site. The metabolites CONH2-fenpropathrin, desphenyl-fenpropathrin, and 4'OH-fenpropathrin were detected in cotton-field soils. There was no vertical movement of the parent compound or metabolites at either field site.

The potential for fenpropathrin to accumulate in the field and contaminate rotational crops was studied at a California and a Mississippi site (Papathakis, 1993). In both studies, five applications of fenpropathrin at the rate of 0.3 lbs ai/acre were performed at 7 day intervals. Lettuce, carrots, and wheat were planted in the test plots 1, 4, and 12 months following the last application. Soil samples were collected at planting and harvest. Crops were sampled at various stages of growth and maturity. No residues were detected in crop samples although fenpropathrin was detected in soil. These data demonstrate that fenpropathrin will not be taken up by crops grown in previously-treated soils.

7. Plant Metabolism

The fate of fenpropathrin and it's metabolites, TMPA and hydrogen cyanide, was studied in several types of plants (Mikami *et al.*, 1985; Papathakis, 1993). Radio-labeled fenpropathrin was applied to actively-growing cabbage plants and maintained under green-house conditions for 42 days. Fenpropathrin and TMPA were applied to apple, cabbage, bean, orange, tomato, and vine foliage samples. Fenpropathrin rapidly penetrated cabbage plants and was metabolized ($t½ = 11\text{-}12$ days). Proposed metabolic pathways include ester bond cleavage, hydrolysis of the cyano group to the $CONH_2$ and COOH groups, hydroxylation at either or both of the *gem*-dimethyl groups with subsequent oxidation to carboxylic acid, and hydroxylation of the phenoxy group. TMPA was converted primarily to malonyl-glucoside. Hydrogen cyanide was released from the cyano group upon hydrolysis of the ester linkage, and rapidly converted into several amino acids and dipeptides that may be subsequently utilized by the plant. Most of the parent compound and metabolites remained at the application area indicating that fenpropathrin does not translocate in plants.

III. TOXICOLOGY PROFILE

A. PHARMACOKINETICS/METABOLISM

Summary

In the rat, approximately 68% of an oral dose of fenpropathrin was excreted in the urine (49%) or feces (16-19%) in the first 24 hours. Comparison of the pharmacokinetic fate of labeled fenpropathrin administered orally, or intraperitoneally, suggested biliary excretion and entero-hepatic reabsorption. Based on the review of the pharmacokinetic data at least 57% of the material is absorbed by the oral route. Dermal absorption of fenpropathrin by rats, corrected for the duration of the study and including the amount of radio-label in the skin, ranged from 18 to 57% of the applied dose, depending upon the concentration applied to the skin. Fenpropathrin did not concentrate in any tissues in the body. The metabolism of fenpropathrin in rats involved cleavage of the ester bond, followed by conjugation with either sulfuric acid or glucuronic acid. Oxidation at the methyl group of the acid moiety, and hydroxylation at the 4' -position of the alcohol moiety occurred prior to cleavage.

1. Rat Oral Studies

Charles River CD rats (6/sex) were given a single oral dose of [^{14}C-benzyl] fenpropathrin (99.5% purity, S.A.=35.9 uCi/mg) at 1.5 mg/kg in corn oil (Crawford and Hutson, 1975). An average of approximately 49% of the administered radio-label was excreted in the urine of males and females in the first 24 hours. An additional 7% of the dose was excreted in the urine during the second 24 hour period. Over the next 5 days, only 2.5 to 4% of the administered dose was excreted in the urine. The fecal excretion pattern was somewhat different. In the first 24 hours, the feces contained an average of 19% (males) or 13% (females) of the administered dose. In the second 24 hours, the feces contained 21% (males) or 18% (females) of the administered dose. In the third 24 hr period, males excreted 7% of the administered dose, and females 3%. No significant fecal excretion was noted after 72 hours. Only 0.005% of the administered dose was eliminated in expired air. Less than 1.5% of the dose remained in the animals eight days after treatment. Fenpropathrin did not concentrate in any tissues. The data were considered supplemental by the Department of Pesticide Regulation (DPR).

Charles River CD male rats (1/dose) were fed a diet containing fenpropathrin (97% purity) at 0 (2 rats as control), 1, 10, 100, or 1000 ppm for 14 days (Creedy and Potter, 1976). Two rats, as positive controls, were fed a diet containing dieldrin (100 ppm) for the same time period. The positive controls exhibited an increase in the mean rate of O-dealkylation of [^{14}C] chlorfenvinphos (0.387 nmol/min-mg wet liver compared to 0.024 nmol/min-mg wet liver for untreated controls), and absolute liver weight (17.2 g compared to 10.8 g for untreated controls). There was no indication of induction of hepatic microsomal enzymes by any concentration of fenpropathrin in the diet. The data were considered supplemental by DPR.

Sprague-Dawley rats (10/sex) were pretreated with 14 daily dosages of 2.5 mg/kg fenpropathrin (99% purity) in corn oil (Savides *et al.*, 1992). On day 15, half of the animals were given [alcohol-^{14}C] fenpropathrin (99.5% purity, 58.1 mCi/mmole), and the other half were given [acid-^{14}C] fenpropathrin (99.5% purity, 74.9 mCi/mmole). There were no significant differences among the groups (label position or sex) with respect to excretion of the administered radio-label. Approximately 45-51% of the administered dose was excreted in the urine in the first 24 hours, and an additional 4-6% was excreted in the second 24 hour period. At the same time, 38-43% were excreted in the feces in the first 24 hours, and 6 to 11% in the second 24 hour period. From 64-78% of the radio-labeled moieties in the feces were metabolites. About 20% of the material was excreted unchanged in the feces. There was no evidence of bioaccumulation. The metabolism of fenpropathrin involved cleavage of the ester bond, followed by conjugation with either sulfuric acid or glucuronic acid. Oxidation at the methyl group of the acid moiety, and hydroxylation at the 4' -position of the alcohol moiety occurred prior to cleavage. The data were considered supplemental by DPR.

2. Rat Oral and Intraperitoneal Studies

[^{14}C-cyclopropyl] fenpropathrin (99.5% purity; 11.8 µCi/mg) was given in a single oral dose of 1.5 mg/kg to six male and six female Charles River CD rats (Crawford and Hutson, 1976). Approximately 35% of the administered radio-label was excreted in the urine and 32% was excreted in the feces during the first 24 hours. In the second part of the study, [^{14}C-benzyl] fenpropathrin (18.1 µCi) was dissolved in 0.1 ml of ethanol and injected intraperitoneally into a single female rat. Approximately 18.3% of the radio-label was collected from the cannulated common bile duct during the first 5.5 hours. At the same time, 8.3% of the dose was collected in the urine. This is indicative that a large proportion of labeled fenpropathrin in the body may be excreted in the feces.

Metabolism by cleavage at the ester bond produced cyclopropanecarboxylic acid and a 3-phenoxybenzyl moiety. Prior to cleavage, half of the dose underwent aryl hydroxylation to form p-hydroxyl-fenpropathrin. Part of this was excreted in the bile as a conjugate, and the other portion was cleaved and eliminated in the urine as a sulfate of 3-(p-hydroxyphenoxy) benzoic acid and as tetramethyl-cyclopropane carboxylic acid glucuronide. A minor portion of the parent compound was hydroxylated at one of the methyl groups of the cyclopropanecarboxylate moiety in the *trans*-orientation to the carboxyl group. The resultant *trans*-hydroxyl-fenpropathrin was eliminated in the bile as a conjugate, and de-conjugated in the feces. Part of this metabolite was cleaved to 2-*trans*-hydroxymethyl-2-methyl-3,3-dimethyl cyclopropanecarboxylic acid that was eliminated in the urine. The study was considered supplemental by DPR.

3. Cow Oral Studies

Two lactating Friesan cows were fed twice daily with a diet containing [^{14}C] fenpropathrin (99.5% purity, 35.8 µCi/mg) at a concentration equivalent to 0.11 µg/g for 21 days (Crayford, 1975). An equilibrium between ingestion and excretion of radio-label was established in five days. Excretion occurred via the urine (48%) and feces

(39%). All milk and tissue samples contained less than 0.01 ppm of [^{14}C]-fenpropathrin. A precise determination of the residues of radio-label in two milk samples indicated a concentration of 0.00026 μg/ml.

4. Rat Dermal Studies

Male Sprague-Dawley (CD/BR) rats (5/termination group/dose group) were given a single dermal application of ^{14}C-fenpropathrin (99% purity, 58.4 mCi/mmol) dosing formulation at 0.00125 mg/cm^2, 0.625 mg/cm^2, or 1.25 mg/cm^2 to a clipped, unabraded 24 cm^2 application site (Johnson *et al.*, 1991). Specific time points analyzed included 0.5, 1, 2, 4, 10, and 24 hours after exposure. The percentages of the applied dose recovered in the urine at 24 hours for the three dosages tested were 18.2, 8.2, and 4.1%, respectively. The percentages of the applied dose recovered in the feces at 24 hours for the 3 dosages tested were 5.8, 1.8, and 0.4%, respectively. At 24 hours, the percentages of the applied dose that remained in the skin at the application site for the three dosages tested were 21.2, 15, and 11.6%, respectively. If it is assumed that 68% of the absorbed dose is excreted in the urine and feces in the first 24 hours (see rat oral studies), then total dose excreted can be estimated. The estimated values for amounts excreted in the urine would be 26.8, 12.1, and 6%, for the three doses. The final amounts excreted in the feces would be 8.5, 2.6, and 0.6%, respectively. If the amount remaining in the skin is also considered absorbed material (U.S. EPA, 1992), then the theoretical total absorbed percentages would be 56.5, 29.7, and 17.6%, respectively.

B. ACUTE TOXICITY

Summary

Clinical signs reported in studies designed to evaluate the acute toxicity of exposure to fenpropathrin included: muscular fibrillation, diarrhea, tremors, ataxia, decreased spontaneous activity, limb paralysis, irregular respiration, salivation, urinary incontinence, loss of righting reflex, hyperpnea, dyspnea, hyperexcitability, convulsions, lacrimation, nasal discharge, erythema and edema. The profile of acute toxicity studies for fenpropathrin technical grade material is summarized in TABLE I. The acute toxicity profile for the proposed formulation containing approximately 31% fenpropathrin is summarized in TABLE II. It should be noted that acute toxicological responses were also reported in long-term (non-acute) studies using fenpropathrin. These effects are reported in the corresponding study sections of this document.

On the basis of the acute profile for fenpropathrin technical grade, as well as the Danitol® and Tame® formulations, the most sensitive route of exposure appears to be the oral route. In the majority of tests, females appeared to be slightly more sensitive than males. The one exception was dermal toxicity in mice where males were 20% more sensitive than females (i.e., the male LD_{50} was 740 mg/kg while the female LD_{50} was 920 mg/kg).

TABLE I: Acute toxicity of technical grade fenpropathrin.

Study/Species	Sex	Result	NOEL	References
Oral LD_{50}				
Sprague Dawley Rats	M/F	71 / 67 mg/kg	10 mg/kg[a]	Hiromori, *et al.*, 1983
Mice (strain unknown)	M/F	67 / 58 mg/kg	30 mg/kg[b]	Kohda and Kadota, 1980a
Rabbits (strain unknown)	M/F	675 / 510 mg/kg	89 mg/kg[c]	Hara, *et al.*, 1980
Subcutaneous LD_{50}				
Sprague Dawley Rats	M/F	1,410 / 900 mg/kg	500 mg/kg[d]	Kohda and Kadota, 1980b
Mice (dd strain)	M/F	1,350 / 900 mg/kg	100 mg/kg[e]	Kohda and Kadota, 1980b
Intraperitoneal LD_{50}				
Sprague Dawley Rats	M/F	225 / 180 mg/kg	50 mg/kg[f]	Kohda and Kadota, 1980b
Mice (dd strain)	M/F	230 / 210 mg/kg	50 mg/kg[g]	Kohda and Kadota, 1980b
Dermal LD_{50}				
Sprague Dawley Rats	M/F	1,600 / 870 mg/kg	100 mg/kg[h]	Kohda, 1979
Mice (strain unknown)	M/F	740 / 920 mg/kg	100 mg/kg[i]	Kohda and Kadota, 1980c
Rabbits (strain unknown)	M/F	> 2,000 mg/kg	2,000mg/kg[j]	Marroquin, 1981
Primary Eye Irritation				
Albino Rabbits	M	Category III		Matsubara *et al.*, 1978
Primary Dermal Irritation				
Albino Rabbits[k]	?	Category IV		Marroquin, 1981

[a] Based on muscular fibrillation, diarrhea, and death occurring within 24 of dosing.
[b] Based on tremors, convulsions, ataxia and death occurring within 24 hours of dosing.
[c] Based on tremors, ataxia, diarrhea, slow respiration and death occurring within 24 of dosing.
[d,e] Based on tremors, hyperexcitability and death occurring within 24 hours of dosing.
[f,g] Based on tremors, decreased spontaneous activity, and muscular fibrillation occurring within 24 hours of dosing.
[h] Based on tremors, hypersensitivity, ataxia, and death occurring within 24 hours of dosing.
[i] Based on tremors, hypersensitivity, and ataxia occurring within 24 hours of the initial dosing.
[j] Based on no significant signs observed in the treatment group.
[k] Due to an incomplete chemical description, the primary dermal irritation study was not acceptable to the Department of Pesticide Regulation (California EPA) as a Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) guideline study. Data from the acute dermal toxicity study supports a toxicity category IV.

Note: Acute inhalation toxicity was not required because the test article has a low melting point and can not be milled to produce an inhalation aerosol.

TABLE II: Acute toxicity of product formulations containing ≈ 31% fenpropathrin.

Study/Species	Sex	Result	Toxicity	References
Oral LD_{50}				
Albino Rats[a]	M	84 mg/kg	Category II	Kiplinger, 1992a
Dermal LD_{50}				
Albino Rabbits	M/F	> 2,000 mg/kg	Category III	Kiplinger, 1992b
Primary Eye Irritation				
Albino Rabbits	?		Category I	Kiplinger, 1992c
Primary Dermal Irritation				
Albino Rabbits	?		Category I	Kiplinger, 1992d

[a] While the LD_{50} for female rats was not determined with the Danitol 2.4 EC formulation, a study with another formulation, S-3206 2.4 EC (also with the 31% active ingredient) established an LD_{50} of 72 mg/kg.

C. SUB-CHRONIC TOXICITY

Summary

The principal adverse effects reported at 7 days or less in studies on laboratory animals were clinical signs from neurotoxicity. The 1-day oral NOEL for clinical signs (emesis, salivation, tremors, and loss of coordination) in dogs was 46 mg/kg. The 5-week oral NOEL for clinical signs in rats was 15 mg/kg/day.

1. Dog Oral Studies

Beagle dogs were dosed with capsules of fenpropathrin (96.2% purity) at 46 (1M, 1F), 100 (2M,2F), 464 (2M, 2F), or 1000 mg/kg/day (2M, 2F) for 21 days (Pence *et al.*, 1979). Large amounts of food emesis, salivation, tremors, and loss of coordination were reported on day 1 for all animals in top 3 dose groups. The 1-day NOEL was 46 mg/kg. No clinical signs were reported in the lowest dose group for 15 days. At the highest dose, one male died on day 2. The objective of the study was to determine the acute oral LD50 in dogs, and to establish tolerable dose levels. The information was considered supplemental.

Beagle dogs (6/sex/group) were fed a diet containing fenpropathrin (96.2% purity) at 0, 250, 500 or 1000 ppm (reduced to 750 ppm after 3 weeks) for 13 weeks (Pence *et al.*, 1980a). The estimated dosages based on food consumption were 0, 7, 15, and 24 mg/kg/day for males and 0, 10, 16, and 29 mg/kg/day for females). Clinical signs, including mucoid stools and/or diarrhea, emesis, tremors and ataxia were initially observed in all dose groups during the second week of exposure. The clinical signs became so severe in the 1000 ppm group by week 3 (one male was terminated in a moribund condition), that the dose was reduced to 750 ppm. After the fifth week, the clinical signs decreased in severity and frequency. There were no treatment related ophthamological effects, no effects on organ weights, and no treatment-related microscopic alterations of any of the organs examined. Except for the high dose group, there was no effect on body weights or food consumption. Due to the lack of test article analysis and the inability to establish a NOEL, the study was unacceptable but possibly upgradeable to DPR as a FIFRA guideline study.

2. Rat Oral Studies

Carworth rats (12 rats/sex/dose) were fed a diet containing fenpropathrin (96% purity) at 2, 10, 50, or 250 ppm for 3 months (Hend and Butterworth, 1975). Controls consisted of 24 rats per sex. No adverse effects were indicated. There were no significant changes in clinical chemistry, hematological indices, or reported pathology. The study was unacceptable to DPR as a FIFRA guideline study because there was no analysis of the diet, dose levels were not sufficiently high, and the target organ was not identified.

Charles River rats (12 rats/sex/dose) were fed a diet containing fenpropathrin (97% purity) at 3, 30, 100, 300, or 600 ppm for 3 months (Hend and Butterworth, 1976). Controls consisted of 24 rats per sex. After 5 weeks of dosing, tremors appeared in 9 females and 1 male at the high dose (600 ppm). The tremors disappeared after 11 weeks. No other groups exhibited clinical signs. Also at 600 ppm the mean body weights were significantly ($P<0.01$) reduced in both males (5-12% of control) and females (8-14% of control). The 5-week NOEL for clinical signs was 300 ppm (approximately 15 mg/kg/day using a default conversion factor (0.05) - Zielhuis and van der Kreek, 1979). At 600 ppm, there were non-significant increases in mean kidney and brain weights, and elevated plasma alkaline phosphatase (but no abnormal histopathology of the liver) for both males and females. The study was unacceptable to DPR as a FIFRA guideline study because there was no analysis of the diet for actual concentration of test compound, and a lack of animal husbandry data.

3. Rabbit Dermal Studies

New Zealand White rabbits (10/sex/group) received fenpropathrin (91.4% purity) at 0, 500, 1200 or 3000 mg/kg/day applied to abraded (50% of animals) or non-abraded skin for 21 days (Riley *et al.*, 1982). Exposure time for each application was 6 hours/day, 5 days a week. No compound-related changes in body weight, food consumption, hematology or biochemical parameters were reported. At termination, no compound-related macroscopic lesions were observed at the application site. Microscopic lesions observed in treated skin were similar in incidence and severity to those in untreated skin. The dermal NOEL for systemic effects was greater than or equal to 3000 mg/kg/day. The study was acceptable to DPR as a FIFRA guideline study.

New Zealand White rabbits (5/sex/dose) were treated dermally with a fenpropathrin formulation (2.4 lb/G EC) at 0, 100, 300, or 900 mg/kg/day in a 6 hr exposure/day, 5 days a week for 3 weeks (Spicer *et al.*, 1982). Dermal findings included erythema, edema, fissuring, atonia and desquamation in all treated groups. Blanching was noted in the 100 and 900 mg/kg/day groups, and coriaceousness in the 900 mg/kg group. In all treated groups there was scabbing, crusting, fissuring or thickening of the skin application site. Acanthosis, hyperkeratosis, abscesses, necrosis, hemorrhage, and ulceration were also reported at the application skin site in intact and abraded rabbits. There were no compound-related differences in body weight, organ weight, hematological or biochemical parameters. There were no adverse systemic effects indicated. The NOEL for systemic effects was greater than or equal to 900 mg/kg/day. The study was unacceptable to DPR as a FIFRA guideline study due to a lack of dosing solution analysis.

D. CHRONIC TOXICITY AND ONCOGENICITY

Summary

No clear indication of oncogenicity was attributed to fenpropathrin in rats or mice. There were no treatment related changes in hematology, clinical chemistry, ophthalmology, gross pathology, or histopathology in rats, mice or dogs. The NOEL for clinical signs (tremors) in dogs was 3 mg/kg/day. The NOEL in rats (based on tremors) was 7.1 mg/kg/day. These effects were observed within a week of initial treatment and were considered a response to acute toxicity.

1. Dog Diet Studies

Beagle dogs (4/sex/dose) were fed a diet containing fenpropathrin (92.5% purity) at 0, 100, 250, or 750 ppm (0, 3, 7, 24.4 mg/kg/day for males; 0, 3, 7.7 24.8 mg/kg/day for females from food consumption data) for one year (Pence *et al.*, 1984). There were no treatment related changes in food consumption, hematology, clinical chemistry, urinalysis, ophthalmology, gross pathology, or histopathology. Tremors, beginning in week 1, were observed consistently in all dogs dosed at 750 ppm (one male found dead in week 32). Ataxia was noted for one 750 ppm male at week 2, and in a different male at week 3. Three 750 ppm males exhibited ataxia in week 6, and two 750 ppm males at week 7. From weeks 8 through 32, ataxia was noted consistently in one or more 750 ppm dogs. From week 33 through the end of the study, ataxia was noted sporadically for one or more 750 ppm dogs. A languid appearance was noted intermittently for one or more 750 ppm dogs from weeks 7 though 48. A languid appearance was not observed in any other dose group. Intermittent tremors, beginning in the second week, were observed in dogs dosed at 250 ppm. The NOEL in dogs for clinical signs (tremors, ataxia, languidity) was 100 ppm (3 mg/kg/day). The study was acceptable to DPR as a FIFRA guideline study.

2. Rat Diet Studies

CD rats (50/sex/dose group with satellite groups of 15 rats/sex/dose) were fed a diet containing fenpropathrin (91.4-92.5% purity) at 0, 50, 150, 450, or 600 ppm (0, 1.9, 5.7, 17, or 22.7 mg/kg/day for males; 0, 2.4, 7.1, 21.9, or 38.8 mg/kg/day for females from consumption data) for up to two years (Warren *et al.*, 1986). All female rats in the 600 ppm dose group were terminated at 52 weeks due to excessive unscheduled mortality in the group. Body tremors were observed starting the first week in both males and females in the 600 ppm dose group, and in females in the 450 ppm dose group. After 14 weeks, females in the 450 ppm dose group exhibited very infrequent tremors. No tremors were seen in the controls or any other dose group. There was no indication of oncogenicity. There were no compound-related effects on food consumption, body weight changes, hematology, clinical chemistry, necropsy, or histopathology findings. The NOEL for tremors in females was 150 ppm (7.1 mg/kg/day). The study was acceptable to DPR under FIFRA guidelines.

3. Mouse Diet Studies

CD-1 mice (52 mice/sex/dose; with satellite groups of 40/sex/dose) were fed a diet containing fenpropathrin (91.4-92.5% purity) at 0, 40, 150, or 600 ppm (0, 3.9, 13.7, or 56 mg/kg/day for males; 4.2, 16.2, 65.2 mg/kg/day for females from consumption data) for 104 weeks (Colley *et al.*, 1985). There was no indication of compound-related oncogenicity in mice. Transient hyperactivity, disappearing by week 78, was reported in some female mice at the 600 ppm dose. There were no treatment-related effects on mortality, body weight gain, organ weights, food consumption, hematological indices, urinalysis, biochemistry, or non-neoplastic lesions. An elevation in number of pulmonary adenocarcinomas was reported in all treatment groups when compared to concurrent controls (the number of adenocarcinomas reported was 1, 6, 12, and 5 for males; and 1, 7, 4, and 5 for females; for 0, 40, 150, and 600 ppm, respectively). Correcting for time to tumor and early death (analysis not shown) did not produce a dose related effect. In the absence of a dose related increase in the number of tumors, and a relatively low background (control) value, a clear indication of oncogenicity could not be attributed to test article exposure. The NOEL for transient hyperactivity in female mice was 16.2 mg/kg/day. This study was acceptable to DPR under FIFRA guidelines.

CD-1 mice (52 mice/sex/dose; with satellite groups of 40/sex/dose) were fed a diet containing fenpropathrin (91.4% purity) at 0, 40, 200, or 1000 ppm (Colley *et al.*, 1982). The study was terminated after 13 weeks of treatment due to high mortality reported among mice receiving 200 or 1000 ppm during the early part of the study. From week 1 onward, males in the 1000 ppm dose group exhibited occasional body tremor. One male in the 200 ppm dose group exhibited tremors beginning in week 2. There were no treatment-related effects on food utilization, and no morphological changes were noted in the histological exams. The study was considered supplemental by DPR.

E. GENOTOXICITY

Summary

A number of studies have been conducted to evaluate the genotoxic activity of fenpropathrin. These studies indicate that the pesticide may have mutagenic potential in the *Salmonella* (Ames test) and the L5178Y mouse lymphoma gene mutation assays. In assays for structural chromosome effects and other genotoxic effects, including DNA damage and repair, genotoxic activity was not indicated for fenpropathrin.

1. Gene Mutation

a) Bacteria

The mutagenic potential of fenpropathrin was evaluated in *Salmonella tryphimurium* and *Escherichia coli* (Izumozaki, *et al.*, 1984). The test was conducted both in the presence and absence of a rat liver metabolizing enzyme system (S-9) in *Salmonella* tester strains TA98, TA100, TA1535, TA1537, and TA1538; and in *E. coli* strain WP2uvrA. The test concentrations included 0, 50, 100, 500, 1000, and 5000 µg/plate. The study was conducted using the pre-incubation methodology (i.e., the test article and the S-9 were pre-incubated for 20 minutes prior to plating onto agar). In the initial study, a dose related increase in the number of revertants was observed in TA100 in the absence of metabolic activation. At 5,000 µg/plate, the number of revertants was greater than two-fold over background (164/78). In a second test, a dose related increase in revertants was also observed, however, the value at 5,000 µg/plate was less than two-fold over background (175/133). Due to the lack of reproducibility of the two-fold increase, the performing laboratory and the initial DPR review did not indicate an adverse effect. However, in light of the dose related increases observed, the mutagenic potential can not be discounted. These studies were considered acceptable by DPR as FIFRA guideline studies.

b) Mammalian Cells

The mutagenic potential of fenpropathrin was evaluated in a mammalian *in vitro* system by Richold *et al.*, (1982a). The study conducted was the mouse lymphoma L5178Y gene mutation assay with and without metabolic activation. Concentrations included 0, 50.3, 84.5 141.9 and 238.2 µg/ml, in dimethyl sulfoxide (DMSO), in the absence of metabolic activation. In the presence of a metabolic activation mixture (S-9) from aroclor 1254 induced rat livers, the test concentrations were 0, 47.5, 75.3, 119.4 and 189.2 µg/ml. In the presence of S-9, a statistically significant increase ($p \leq 0.05$) in mutation frequency, when compared to control values, was observed at the two highest concentrations (144/79 and 139/79). Due to the lack of a confirming assay, DPR did not consider this study acceptable as a FIFRA guideline study. In the absence of additional information, however, the data suggest that fenpropathrin may have mutagenic potential in this system.

c) Eucaryotic Microorganisms

The genotoxic potential of fenpropathrin on microbial cells implanted in a host animal was investigated by Brooks (1980). For this host-mediated assay, male CF (Carworth Farm) mice were orally treated with fenpropathrin in DMSO at 0, 10, or 20 mg/kg. They were subsequently injected intraperitoneally with a culture of yeast cells (*Saccharomyces cerevisiae*). Five hours after dosing the mice were killed and the yeast cells were harvested and analyzed for mutation induction. No indication of induced mutation was reported. This study was not, however, considered acceptable to DPR as a FIFRA guideline study.

2. Structural Chromosomal Aberration

a) In Vivo cytogenetics

The effect of fenpropathrin on chromosomes was evaluated by the mouse micronucleus test by Hara and Suzuki (1984a). Fenpropathrin was administered to six week-old male ICR mice by intraperitoneal injection. Dosages were 0, 50, 100, and 200 mg/kg. No increase in micronucleated bone marrow cells was reported. Under the conditions of this study, fenpropathrin exposure is not associated with chromosomal abnormalities in mice. This study was considered unacceptable to DPR as a FIFRA guideline study.

The potential of fenpropathrin to induce chromosomal abnormalities in bone marrow cells from Chinese hamster was investigated by Dean (1975). For this study, 48 male and female animals were treated, in two successive daily oral doses, with 0, 10, or 20 mg/kg fenpropathrin in DMSO. Under the conditions of this study, fenpropathrin did not induce chromosomal abnormalities in Chinese hamster bone marrow cells. Due to a number of deficiencies, this study was not, however, considered acceptable to DPR as a FIFRA guideline study. The deficiencies included the following: individual data were not presented, the mitotic index was not reported, no justification for dose selection was presented, the criteria for scoring was not given.

b) In Vitro cytogenetics

The potential of fenpropathrin to induce chromosomal aberrations in when treatment is *in vitro* was investigated by Kogiso, *et al.* (1989). The test was conducted both in the presence and absence of a rat liver S-9 metabolic activation mixture. In addition to untreated and solvent (DMSO) controls, the test was conducted at fenpropathrin concentrations of 10, 15, 20, 25, and 30 μg/ml. Concentrations in excess of these were too toxic for evaluation. Exposure times included 2, 18 and 24 hours. No increase in aberrations was attributed to fenpropathrin. This study was considered acceptable to DPR as a FIFRA guideline study.

3. Other Genotoxic Effects

a) DNA Damage

The effect of fenpropathrin on DNA damage and repair was investigated by Richold, *et al.* (1982b). Using auto-radiographic techniques, fenpropathrin was tested in HeLa S3 cells both in the presence and absence of a S-9 metabolic activation mixture. No indication of DNA damage was reported. The results were, however, suspect in that positive controls were marginal. The study was considered acceptable by DPR as a FIFRA guideline study.

The potential of fenpropathrin to induce DNA damage, as implied by induction of differential lethality in DNA repair-deficient bacteria, was investigated by Kishida, *et al.* (1980). Using wild type and repair-deficient *Bacillus subtilis*, no differential toxicity was observed at concentrations ranging from 0 to 5,000 μg/disk. Due to a lack of a metabolic activation test, this study was considered unacceptable to DPR as a FIFRA guideline study.

b) Sister Chromatid Exchange

The potential of fenpropathrin to induce sister chromatid exchanges was studied by Hara and Suzuki (1984b). The study was conducted in Chinese hamster ovary (CHO-K1) cells in the presence and absence of rat liver S-9 (metabolic activation mixture). Concentrations ranged from 0 to 3 x 10^{-4} M. Fifty cells per dose were evaluated for the induction of sister chromatid exchanges. No induction of sister chromatid exchanges were reported. This study was considered acceptable to DPR as a FIFRA guideline study.

F. REPRODUCTIVE TOXICITY

Summary

Major clinical signs reported in studies designed to evaluate the reproductive toxicity potential of fenpropathrin included maternal tremors and death, neonatal tremors and death, and decreased litter size (attributed to increased pup mortality). These effects were considered to be related to acute toxicity.

1. Rat Oral Studies

A three generation reproduction study was conducted to evaluate the effects of fenpropathrin on COBS (cesarean originated barrier maintained) male and female rats (Hend, *et al.*, 1979). The test article concentrations included 0, 5, 25 and 250 ppm and was administered in the diet. The Fo generation dosages were approximately 0, 0.44, 2.1, and 21 mg/kg/day for males, and 0, 0.36, 1.8, and 18 mg/kg/day for females. Both the maternal and developmental NOELs were considered to be greater than the highest dose tested. This study was not, however, considered acceptable to DPR as a FIFRA guideline study, due to insufficient dose level selection.

The effect of fenpropathrin on multiple generations of rats was investigated by Cozens, *et al.*, (1986). The exposures for this study were 0, 40, 120, or 360 ppm fenpropathrin in the diet. The Fo generation dosages were approximately 0, 2.6, 7.8, and 23 mg/kg/day for males, and 0, 3.1, 9.1, and 28 mg/kg/day for females. Exposure was to 17 to 28 animals per sex per group per parental generation. In this 3 generation study, no effect on mating performance of surviving animals was reported. Furthermore, no mortalities were reported among male animals. In the 360 ppm dose group, 18 females died with 10 of the deaths occurring in the F1b females during lactation. On the basis of average food consumption, the estimated dosage for this group was 35 mg/kg/day. During the second and third week postpartum, females in this dose group exhibited body tremors with associated spasmodic muscle twitches and increased sensitivity. Pup mortality at the second mating of the Fo animals and at both matings of the F1b animals increased in the 360 ppm group. The cumulative pup loss in the Fo animals was 11.1 % for the 360 ppm group and 3.3 % in the controls. In the F1b 1st mating, the loss was 5.8 % for the 360 ppm and 1.3 % in controls. At the second mating for the F1b animals the 360 ppm pup loss was 10.2 % while the control value was 3.3 %. At 120 ppm, 2 F1b females died during lactation, 1 F1b female exhibited tremors and muscle twitches, as well as, increased sensitivity during the second week postpartum. Three F2b pups in the dose group exhibited body tremors prior to weaning. Two of these animals died. Clinical signs at the 40 ppm level were considered similar to that of the control animals. The systemic NOEL for this study was 40 ppm (3.1 mg/kg/day) based on maternal tremors and deaths, and on tremors in F2b pups. The paternal NOEL was considered ≥ 360 ppm (23 mg/kg/day), as there was no effect at the highest dose tested. The reproductive NOEL was considered to be 120 ppm (9.1 mg/kg/day), based on decreased litter size (due to increased pup mortality). This study was considered acceptable to DPR as a FIFRA guideline study.

G. DEVELOPMENTAL TOXICITY

Summary

The following studies were performed to evaluate the developmental toxicity potential of fenpropathrin. Investigations were performed in both rats and rabbits. No fetal abnormalities were attributed to the test article in either animal. On the basis of these studies, fenpropathrin was not fetotoxic up to 10 mg/kg/day in Fischer 344 rats or up to 36 mg/kg/day in rabbits. Severe effects were, however, reported. In rats, neurologic effects were reported throughout the treatment groups with significant effects (including death) reported at doses greater than 6 mg/kg/day. The NOEL used in the risk characterization for acute effects in greenhouse mixer/loader and applicators was 6 mg/kg/day.

1. Rat Oral Studies

A study of the embryotoxic and teratogenic effects of fenpropathrin on Fischer 344 rats was reported by Pence, *et al.*, (1980b). In this study, technical grade fenpropathrin was administered, by oral intubation, on days 6 through 15 of gestation to each of 4 groups of approximately thirty female rats. The dose levels were 0, 0.4, 2, and 10 mg/kg (body weight) /day. The 0 dose group received only corn oil (vehicle). Tremors were observed on the first day of compound administration and once again during the treatment period in the high dose animals. Nine animals in the 10 mg/kg dose group were found dead. All deaths occurred within the first 8 days of the treatment regimen. One animal in the 2 mg/kg dose group was also found dead. This death occurred 8 days after the initial administration of fenpropathrin. A decrease in body weight gain (73% of control, $p<0.05$) and food consumption (85% of control value, $p<0.05$) was also reported at the 10 mg/kg dose. On the basis of premature death, the maternal NOEL for this study was 0.4 mg/kg. No fetal abnormalities were attributed to administration of fenpropathrin in this study. The developmental NOEL for this study was ≥ 10 mg/kg, the highest dose tested. At the initial data review, DPR considered this study unacceptable but possibly upgradeable due to a lack of dose analysis. After further review, the DPR position is that this study is not of sufficient quality for regulatory purposes.

A second study addressing the potential teratogenic effects of fenpropathrin on Fischer 344 rats was reported by Morseth (1990). In this study, the test material was administered to each of 7 groups of thirty female rats. Administration was by oral intubation on days 6 through 15 of gestation. The dose levels included were 0, 0.4, 1.5, 2, 3, 6, and 10 mg/kg (body weight). The control group received corn oil (vehicle). Seven animals in the 10 mg/kg dose group were found dead or moribund (6 found dead). These deaths occurred between day 1 and 7 of the treatment regimen. A decrease in body weight gain (87% and 70% of control, $p<0.05$) was reported at the 6 and 10 mg/kg dosages, respectively. On the basis of body weight change, the maternal NOEL for this study was 3 mg/kg. For this risk assessment, the maternal NOEL for acute toxicity was assumed to be 6 mg/kg, based on tremors and deaths. No fetal abnormalities were attributed to administration of fenpropathrin in this study. The developmental NOEL for this study was ≥ 10 mg/kg, the highest dose tested. DPR considered this study acceptable as a FIFRA guideline study.

2. Rabbit Oral Studies

The teratogenic potential of fenpropathrin was investigated in New Zealand white rabbits (Cozens, *et al.*, 1985). The test article was administered to pregnant females at dosages of 0, 4, 12, and 36 mg/kg/day. Seventeen to 19 females per dosage group were used. Dosing began on day 7 of gestation and continued daily until day 19. One rabbit died in the high dose group. Two rabbits in this group exhibited tremors following dosing. On the basis of these observations, the maternal NOEL for this study was 12 mg/kg/day. No developmental effects were attributed to exposure to fenpropathrin. The developmental NOEL for this study is, therefore, ≥ 36 mg/kg/day (the highest dose tested). This study was considered acceptable to DPR as a FIFRA guideline study.

The teratological potential of fenpropathrin was investigated in Dutch rabbits (van der Pauw, *et al.*, 1980). Twenty to 31 females were administered the test article in gelatin capsules on days 6 through 18 of gestation. The dosages were 0, 1.5, 3, and 6 mg/kg/day. No adverse effects were indicated. The study had a number of deficiencies that inhibited interpretation. The deficiencies included: no justification of dose selection; no in-life observations reported for food consumption and animal husbandry. DPR did not considered this study acceptable as a FIFRA guideline study.

H. NEUROTOXICITY

Hens (6/group) were given 5 successive (unprotected by atropine) daily doses of 1 g/kg of fenpropathrin (96% purity), vehicle (dimethyl sulfoxide), or tri-ortho-tolyl phosphate (0.5 mg/kg) as a positive control (Milner and Butterworth, 1977). There were no mortalities. (The fenpropathrin LD_{50} for hens is 1.5 g/kg). Hens in the positive control group exhibited signs of neurological disturbances by the 16th day after dosing. The signs became progressively worse over the following 9 days, with histological examinations revealing degeneration of the myelin and swollen axons in the sciatic nerve. There was also degenerating myelin in the spinal cord. Negative controls and hens treated with fenpropathrin exhibited no signs of neurological disturbance, and no histological lesions were found. The study was considered supplemental by DPR.

IV. RISK ASSESSMENT

A. HAZARD IDENTIFICATION

1. Acute Toxicity (24 hours or less)

Clinical signs reported in studies designed to evaluate the acute effects of exposure to fenpropathrin included: muscular fibrillation, diarrhea, tremors, ataxia, decreased spontaneous activity, limb paralysis, irregular respiration, salivation, urinary incontinence, loss of righting reflex, hyperpnea, dyspnea, hyperexcitability, convulsions, lacrimation, nasal discharge, erythema and edema. Summaries of acute toxicity studies for fenpropathrin technical grade material and the proposed formulation were presented in TABLES I and II, respectively. Acute toxicological responses (primarily tremors and premature death) were also reported in sub-chronic and chronic studies with dogs and rats, reproductive studies in rats, and developmental studies in rats.

On the basis of the acute exposure profile for fenpropathrin, the most sensitive route of exposure appears to be oral. In the majority of tests, females appeared to be slightly more sensitive than males. Acute NOELs for fenpropathrin have been selected for both the oral and dermal routes of exposure. The acute dermal NOEL of 100 mg/kg was derived from acute dermal LD_{50} studies conducted in rats and mice (Kohda, 1979; and Kohda and Kadota, 1980c, respectively). In both studies, the NOELs were based on ataxia, tremors and hypersensitivity. After correcting for dermal penetration (32%), the NOEL used for acute dermal exposure was 32 mg/kg/day. The acute oral NOEL of 6 mg/kg was derived from a rat developmental study (Morseth, 1990). Death, convulsions, ataxia and tremors occurred in this study between days one and seven in rats treated with 10 mg/kg/day. This NOEL (6 mg/kg) was used in the margin of safety calculation for acute dietary exposures. Since an acute inhalation study was not conducted with fenpropathrin, the acute oral NOEL (6mg/kg) was used. The oral NOEL was not adjusted for possible incomplete absorption from the gastro-intestinal tract, because the pharmacokinetic data were insufficient to accurately determine a quantitative adjustment factor.

For Danitol®, margin of safety calculations for acute worker exposure included two routes (dermal and dietary) and two NOELs (32 and 6 mg/kg). For Tame®, margin of safety calculations for mixer/loader and harvester acute exposures involved three routes (dermal, dietary, and inhalation). A NOEL of 32 mg/kg was used for dermal exposure while 6 mg/kg oral NOEL was used for dietary and as a surrogate for inhalation. With harvesters involved with the use of Tame®, inhalation exposure was assumed to be insignificant. Margin of safety calculations for this occupational group, therefore, involved two routes of exposure (dermal and dietary) and two NOELs (32 and 6 mg/kg).

2. Short-term Toxicity (1 to 3 weeks)

Clinical signs have also been reported in animals following short-term exposures to fenpropathrin. In a chronic feeding study, female dogs administered 7.7 mg/kg/day fenpropathrin exhibited tremors, ataxia, and languidity within two weeks of initial dosing (Pence *et al.*,1984). The NOEL established from this study was 3 mg/kg/day. This NOEL for short-term exposure was supported by clinical signs observed in the second week of a reproductive study conducted with rats. In that study a NOEL of 3.1 mg/kg/day was established based on tremors and deaths observed at 9.1 mg/kg/day. Due to the absence of adequate short-term studies for dermal, inhalation and dietary exposures, 3 mg/kg/day was used in calculating a margin of safety for all short-term expose scenarios.

3. Chronic Toxicity

Chronic occupational exposure to fenpropathrin may occur as workers perform their tasks on an annual basis as well as over lifetime. Estimates for chronic exposure can be determined by multiplying the potential acute dosage by the number of exposure days and dividing by the total number of days in the time period. Chronic dietary exposures may occur as people consume commodities containing residues of fenpropathrin on an annual basis as well as over a lifetime. While acute exposure estimates take into account maximum potential exposure, chronic exposure is more likely to reflect a central tendency (e.g., average). Chronic exposure estimates, therefore, are generally significantly less than acute estimates (absorbed daily dosage or ADD). Based on this assumption, and the fact that the current data base for fenpropathrin does not indicate chronic toxicity potential, this risk assessment does not quantitatively assess chronic exposure. It is assumed that pesticide usage that results in adequate protection for acute and short-term exposures will be sufficient for chronic exposures.

4. Oncogenicity

No clear evidence for oncogenic effects have been reported for fenpropathrin. This pesticide is not, therefore, considered an oncogen at this time.

5. Genotoxicity

The current data base for genotoxicity indicates that fenpropathrin may have mutagenic potential in the *Salmonella* (Ames test) and the L5178Y mouse lymphoma gene mutation assays. In assays for structural chromosome effects and other genotoxic effects, including DNA damage and repair, genotoxic activity was not reported. In the absence of clear evidence for oncogenicity and/or chronic toxicity, the biological impact of these data are unknown.

B. EXPOSURE ASSESSMENT

1. Occupational Exposure

Summary

Occupational related exposure to fenpropathrin was evaluated by the Worker Health and Safety branch of DPR (Dong, 1994). Exposure scenarios considered for this assessment reflect the intended uses under a Section 3 registration, i.e., Danitol® for cotton and Tame® for greenhouse crops. For Danitol®, both aerial and ground application scenarios were considered. For aerial application, occupational activities included mixer/loaders, pilots and flaggers. For ground application, mixer/loaders, applicators and cotton scouts (field checkers) were considered. Exposure to mixer/loaders considered both open pour and closed pour systems. For Tame®, mixer/loaders, applicators, and harvesters were evaluated for exposure.

a) Acute Exposure

Danitol® (cotton)

The acute dermal exposure estimates and the corresponding absorbed daily dosages, for the various occupational activities involved with the treatment of cotton, are presented in TABLE III. The values represent potential average and maximum exposures. Also indicated is the sample size used in determining the exposure values. Since actual exposure data for fenpropathrin were not available, the dermal exposures were based on exposure rates for other pesticides compiled in a U.S. EPA draft document (Lunchick, 1988) and reported by Dong (1994). The absorbed dosage assumed a dermal absorption of 32% and a body weight of 76 kg. The dermal absorption of 32% was assumed from the 10 hour time point of a study conducted with rats (Johnson *et al.*, 1991). Based on a low vapor pressure and surrogate data indicating less than 1% adsorbed dosage, the inhalation exposure was assumed to be negligible (Dong, 1994). As indicated in TABLE III, the average absorbed daily dosages ranged from 0.80 to 24.04 μg/kg/day. The occupation with the highest potential exposure was cotton scouts. The absorbed daily dosages based on maximum potential exposure ranged from 2.24 to 57.09 μg/kg/day. The occupation with the highest potential exposure in this case was also cotton scouts.

TABLE III: Potential daily exposure and absorbed daily dosages for workers involved in the treatment of cotton with fenpropathrin (Danitol®).

Occupational Activity	Dermal Exposure[a] (μg/day)	Sample Size	Absorbed Daily Dosage[b] (μg/kg/day)
Aerial Application			
Mixer/Loaders[c]	16 (45)	13	5.12 (14.4)
Pilots	5 (16)	12	1.47 (5.05)
Flaggers	13 (75)	11	4.00 (24.00)
Ground Application			
Mixer/Loaders[c]	3 (7)	13	0.80 (2.24)
Applicators	10 (76)	15	3.12 (24.21)
Cotton Scouts[d]	75 (178)	N/A	24.04 (57.09)

[a] Values for worker exposure were based on surrogate data, i.e., a pesticide data base compiled in a U.S. EPA draft document (Lunchick, 1988). The values presented represent the mean and maximum (in parenthesis) calculated values, based on the maximum labeled application rate (see Dong 1994).

[b] based on assumed dermal absorption of 32% and male body weight of 76 kg. Inhalation exposure is assumed to be negligible for Danitol® based on low vapor pressure and surrogate data indicating less than 1% (Dong, 1994).

[c] Based on a closed pour system.

[d] based on the dislodgeable foliar residues data obtained from application of Danitol to grapes, and transfer factors derived from field studies (Dong, 1994).

Tame® (greenhouse crops)

The dermal and inhalation exposure estimates and the corresponding absorbed daily dosages, for the various occupational activities involved with the treatment of greenhouse crops, are presented in TABLE IV. As with the previous table, the values represent potential average and maximum exposures based on the maximum labeled application rate (Dong 1994). Mixer/loader values were based on assumptions used for cotton, applicator estimates were based on dermal exposure from a fluvalinate study, and harvester exposure was based on a transfer rate from studies with chlorothalonil and thiophanatemethyl, and dislodgeable foliar residues from a study of fenpropathrin on grape leaves (see Dong, 1994 for a complete discussion of estimated exposures). The absorbed daily dosage assumed a dermal absorption of 32% and an average male/female body weight of 68.7 kg (The body weight was averaged because the surrogate data contained both males and females). The inhalation exposure for mixer/loaders and applicators was based on data from Stamper *et al.*, (1989) and described by Dong (1994). The exposure estimate was 1.2 µg/kg/day. Assuming 50% absorption, the absorbed dosage from inhalation was 0.6 µg/kg/day. For harvesters, the inhalation exposure was assumed to be insignificant. As indicated, the absorbed daily dosages, based on mean exposure ranged from 0.95 to 29.74 µg/kg/day. The occupation with the highest potential exposure was harvesters. The absorbed daily dosages based on maximum potential exposure ranged from 2.15 to 44.60 µg/kg/day. The occupation with the highest potential exposure in this case was also harvesters.

TABLE IV: Potential daily exposure and absorbed daily dosages for workers involved in the treatment of greenhouse crops with fenpropathrin (Tame®).

Occupational Activity	Dermal Exposure (µg/kg/day)[a,b]	Inhalation Exposure (µg/kg/day)[b,c]	Absorbed Daily Dosage (µg/kg/day)
Mixer/Loaders[b]	1 (5)	1.2	0.95 (2.15)
Applicators	34 (98)	1.2	11.48 (31.92)
Harvesters	93 (139)	0	29.74 (44.60)

[a] values presented represent the mean and maximum (in parenthesis) predicted values, based on the maximum labeled application rate (Dong 1994). Mixer/loader values were based on assumptions used for cotton, applicator estimates were based on dermal exposure from a fluvalinate study, and harvester exposure was based on a transfer rate from studies with chlorothalonil and thiophanatemethyl and dislodgeable foliar residues from a study of fenpropathrin on grape leaves (see Dong, 1994 for a complete discussion of estimated exposures).

[b] based on assumed dermal absorption of 32% and an averaged male/female body weight of 68.7 kg

[c] inhalation exposure was based on an assumed 50% absorbed dosage (Dong, 1994). harvester inhalation exposure assumed to be insignificant.

b) Short-Term Exposure

Inasmuch as agricultural practices present the likelihood that workers would treat crops on multiple days, a short-term exposure scenario is being considered for this risk assessment. For this document, short-term exposure is defined as the exposure a worker might receive in the use of fenpropathrin products for a 1 to 3 week period (e.g., as a result of treating multiple crops). The absorbed daily dosage for short-term exposure, for each occupational activity, can be determined by multiplying the potential acute dosage (ADD) (see TABLES III and IV) by the number of exposure days (6 days per week) and dividing by the number of days in the time period (7 days). These values along with an estimate of dietary exposure are presented in the combined occupational and dietary exposure section (TABLES XI and XII).

2. Dietary Exposure

DPR evaluates the risk of exposure to an active ingredient in the diet using two processes: (1) use of residue levels detected in foods to evaluate the risk from total exposure, and (2) use of tolerance levels to evaluate the risk from exposure to individual commodities (see the Tolerance Assessment of this document). For the evaluation of risk to detected residue levels, the total exposure in the diet is determined for all label-approved raw agricultural commodities, processed forms, and animal products (meat and milk) that have established U.S. EPA tolerances. Tolerances may be established for the parent compound and associated metabolites. DPR considers these metabolites and other degradation products that may be of toxicological concern in the dietary assessment.

a) Residue Data

The sources of residue data for dietary exposure assessment include DPR and federal monitoring programs, field trials, and survey studies. In the absence of data, surrogate data from the same crop group as defined by U.S. EPA or theoretical residues equal to U.S. EPA tolerances are used. Residue levels that exceed established tolerances (over-tolerance) are not utilized in the dietary exposure assessment because over-tolerance incidents are investigated by the DPR Pesticide Enforcement Branch and are relatively infrequent. DPR evaluates the potential risk from consuming commodities with residues over tolerance levels using an expedited acute risk assessment process.

DPR has four major sampling programs: (1) priority pesticide, (2) preharvest monitoring, (3) produce destined for processing, and (4) marketplace surveillance. The priority pesticide program focuses on pesticides of health concern as determined by DPR Enforcement and Medical Toxicology Branches. Samples are collected from fields known to have been treated with the specific pesticides. For the marketplace surveillance program, samples are collected at the wholesale and retail outlets, and at the point of entry for imported foods. The sampling strategies for both priority pesticide and marketplace surveillance are similar and are weighted toward such factors as pattern of pesticide use; relative number and volume of pesticides typically used to produce a commodity; relative dietary importance of the commodity; past monitoring results; and extent of local pesticide use. The preharvest monitoring program routinely examines the levels of pesticides on raw agricultural commodities in the field at any time during the growth cycle. Generally, these data are not used unless the application schedule is known and residue data are not available from other monitoring programs. Commodities destined for processing are collected in the field no more than 3 days prior to harvest, at harvest, or post-harvest before processing.

The United States Food and Drug Administration (FDA) has three monitoring programs for determining residues in food: (1) regulatory monitoring, (2) total diet study, and (3) incidence/level monitoring. For regulatory monitoring, surveillance samples are collected from individual lots of domestic and imported foods at the source of production or at the wholesale level. In contrast to the regulatory monitoring program, the total diet study monitors residue levels in the form that a commodity is commonly eaten or found in a prepared meal. The incidence/level monitoring program is designed to address specific concerns about pesticide residues in particular foods.

The U. S. Department of Agriculture (USDA) is responsible for the Pesticide Data Program (PDP), a nationwide cooperative monitoring program. The PDP is designed to collect objective, comprehensive pesticide residue data for risk assessments. Several states, including California, collect samples at produce markets and chain store distribution centers close to the consumer level. The pesticide and produce combinations are selected based on the toxicity of the pesticide as well as the need for residue data to determine exposure. In addition, USDA is responsible for the National Residue Program which provides data for potential pesticide residues in meat and poultry. These residues in farm animals can occur from direct application, or consumption of commodities or by-products in their feed.

In the case of fenpropathrin, surveillance data are not available. With a minimum detection limit of 0.2 ppm, DPR has monitored for residues in tomatoes (in connection with a Section 18 registration) but has not detected fenpropathrin (CDFA, 1991). The FDA has monitored for (with a limit of quantification (LOQ) of 0.02 ppm) and has not found any residues of fenpropathrin in 1991, 1992, or 1993 (FDA, 1993). The USDA has not monitored for fenpropathrin (USDA 1991 and USDA 1992). In estimating dietary exposure of fenpropathrin, residue data were obtained from registrant supplied field trials for cotton and tomatoes. Cotton was considered as part of the current Section 3 registration petition. Tomatoes were considered because of a current Section 18 registration. In addition to cotton seed oil, which is used in cooking, cotton byproducts (meal, seeds, hulls, and soapstock) are used in the feed of domestic farm animals. It was necessary, therefore, to consider the potential of fenpropathrin residues in meat, fat, milk, poultry, and eggs. The residue values used for meats and byproducts were extrapolated either from field study data or tolerance levels (see APPENDIX C for details). The residue values used in the dietary portion of this risk assessment are presented in TABLE V.

TABLE V: Summary of residue values for fenpropathrin used in the dietary risk assessment for fenpropathrin.

Commodity	Residue (ppm)	Data Source	Reference
Cotton Seed	0.29	field study	(Fujie, 1990)
Cattle, Sheep, Swine			
(fat)	0.02	tolerance	(U.S. EPA 1993)
(meat)	0.01	field study	(Fujie, 1986a)
(meat by-products)	0.01	field study	(Fujie, 1986a)
(whole milk)	0.01	field study	(Fujie, 1986a)
(milk fat)	0.03	tolerance	(U.S. EPA 1993)
Horse	0.01	tolerance	(U.S. EPA 1993)
Poultry			
(eggs)	0.01	field study	(Fujie, 1986b)
(fat)	0.02	tolerance	(U.S. EPA 1993)
(meat)	0.01	field study	(Fujie, 1986b)
(meat by-products)	0.01	field study	(Fujie, 1986b)
Tomatoes	0.07	field study	(Lai, 1990)

b) Acute (Daily) Exposure

Estimates of potential acute (daily) dietary exposure use the highest measured residue values at or below the tolerance for each commodity. The following assumptions were used to estimate potential acute dietary exposure from measured residues: 1) the residue does not change over time, 2) the concentration of residue does not decrease when the raw agricultural commodity (RAC) is washed, 3) processing of RACs into various food forms does not reduce the residue, and 4) all foods that are consumed will contain the highest reported residue.

Acute dietary exposure analyses were conducted using the Exposure-4™ computer program developed by Technical Assessment Systems, Inc. (TAS, 1992). This software estimates the distribution of single-day exposures for the overall U.S. population and specific population sub-groups. The analysis utilizes food consumption data, as reported by the U.S. Department of Agriculture (USDA, 1988). Exposure-4™ is designed to evaluate exposure to chemical residues as a function of consumer-days. A consumer-day is any day in which at least one commodity is consumed.

For the population subgroups examined, the potential acute dietary dosage of fenpropathrin from exposure to cotton products ranged from 0.204 to 0.986 μg/kg body weight /day (see TABLE VI for summary data). The population subgroup with the highest potential dosage (0.986 μg/kg body weight /day) was non-nursing infants less than 1 year of age. Estimated dosages were based on the 95th percentile of consumer-day exposures.

TABLE VI: Potential acute dietary exposure to fenpropathrin from residues in cotton.

Population Sub-group	Dosage (μg/kg body wt/day)[a,b]
U.S. Population	0.446
Western Region - U.S. Population	0.439
Nursing Infants (< 1 year)	0.278
Non-Nursing Infants (< 1 year)	0.986
Females (13 + /P[c]/NN[d])	0.245
Females (13 + N[e])	0.335
Children (1-6 years)	0.875
Children (7-12 years)	0.562
Males (13-19 years)	0.334
Females (13-19 years/NP[f]/NN)	0.314
Males (20+ years)	0.227
Females (20 + /NP/NN)	0.204
Seniors (55 + years)	0.213
U.S. Population (16 + years)	0.225

a = Exposure is evaluated as a function of user-days (i.e., day which at least one commodity, containing fenpropathrin is consumed).
b = Values represent the 95th percentile of consumer-day exposure.
c = pregnant
d = not nursing
e = nursing
f = not pregnant

For the population subgroups examined, the potential acute dietary dosage of fenpropathrin from exposure to tomato products ranged from 0.327 to 1.251 µg/kg body weight /day (see TABLE VII for summary data). The population subgroup with the highest potential dosage (1.251 µg/kg body weight /day) was children ages 1 to 6.

TABLE VII: Potential acute dietary exposure to fenpropathrin from residues in tomatoes.

Population Sub-group	Dosage (µg/kg body wt/day)[a,b]
U.S. Population	0.653
Western Region - U.S. Population	0.691
Nursing Infants (<1 year)	0.327
Non-Nursing Infants (<1 year)	1.094
Females (13+/P[c]/NN[d])	0.457
Females (13+N[e])	0.464
Children (1-6 years)	1.251
Children (7-12 years)	0.820
Males (13-19 years)	0.602
Females (13-19 years/NP[f]/NN)	0.497
Males (20+ years)	0.459
Females (20+/NP/NN)	0.399
Seniors (55+ years)	0.357
U.S. Population (16+ years)	0.439

a = Exposure is evaluated as a function of user-days (i.e., day which at least one commodity, containing fenpropathrin is consumed).
b = Values represent the 95th percentile of consumer-day exposure.
c = pregnant
d = not nursing
e = nursing
f = not pregnant

As indicated, the above dietary exposure estimates were based on consumer-day exposure, i.e., an individual was considered if he or she consumed the commodity on the day in question. When multiple commodities are being considered, individuals with the highest exposure from a single commodity may or may not be in upper percentiles of exposure for other commodities. In other words, upper percentile exposures are not additive. TABLE VIII presents the predicted 95th percentile dosage to various population subgroups when exposure is through residues from both cotton and tomato products. The predicted dosages ranged from 0.416 to 1.306 µg/kg body weight /day. The population subgroup with the highest potential dosage (1.306 µg/kg body weight /day) was children ages 1 to 6.

TABLE VIII: Potential acute dietary exposure to fenpropathrin from residues in cotton and tomatoes.

Population Sub-group	Dosage (μg/kg body wt/day)[a,b]
U.S. Population	0.729
Western Region - U.S. Population	0.773
Nursing Infants (<1 year)	1.094
Non-Nursing Infants (<1 year)	1.166
Females (13+/P[c]/NN[d])	0.499
Females (13+N[e])	0.472
Children (1-6 years)	1.306
Children (7-12 years)	0.914
Males (13-19 years)	0.672
Females (13-19 years/NP[f]/NN)	0.568
Males (20+ years)	0.511
Females (20+/NP/NN)	0.443
Seniors (55+ years)	0.416
U.S. Population (16+ years)	0.490

a = Exposure is evaluated as a function of user-days (i.e., day which at least one commodity, containing fenpropathrin is consumed).
b = Values represent the 95th percentile of consumer-day exposure.
c = pregnant
d = not nursing
e = nursing
f = not pregnant

c) Short-Term Exposure

The average daily dietary exposure to fenpropathrin for short-term exposure (1 to 3 weeks) to fenpropathrin is assumed to be the same as the estimates for acute, single day exposure.

3. Combined Exposure (Occupational and Dietary)

a) Acute Exposure

Both potential occupational and dietary exposures to fenpropathrin from Danitol® are presented in TABLE IX. For the purposes of this document, acute exposure is defined as exposure of 24 hours or less. For the dietary component of exposure, residues from cotton and tomato related commodities are considered. Cotton is considered because of the intended use in California, and tomatoes because of potential use under a current Section 18 registration. The population subgroup used for dietary exposure was the "U.S. Population ages 16 and older". This group was chosen as a reasonable representation of potential workers. As indicated in the table, the occupation with the highest predicted exposure was cotton scouts. Their estimated average dosage, expressed as absorbed daily dosage for combined exposures, was 24.53 μg/kg body weight /day. Their estimated maximum dosage was 57.58 μg/kg body weight /day.

TABLE IX: Combined occupational and dietary acute exposure to fenpropathrin from the use of Danitol® on cotton.

	Absorbed Daily Dosage (μg/kg/day)		
Occupational Activity	**Occupational[a]**	**Dietary[b]**	**Combined[a]**
Aerial Application			
Mixer/Loader	5.12 (14.45)	0.49	5.61 (14.94)
Pilots	1.47 (5.05)	0.49	1.96 (5.54)
Flaggers	4.00 (24.00)	0.49	4.49 (24.49)
Ground Application			
Mixer/Loader	0.80 (2.24)	0.49	1.29 (2.73)
Applicators	3.12 (24.21)	0.49	3.61 (24.70)
Cotton Scouts	24.04 (57.09)	0.49	24.53 (57.58)

[a] values represent the mean and maximum (in parenthesis).
[b] exposure of U.S. population (16 years +) to cotton related byproducts, tomatoes, and tomato byproducts.

Both occupational and dietary exposure to fenpropathrin from Tame®, the product to be used in greenhouse crops, are presented in TABLE X. As with the cotton workers (Danitol®), the dietary component of the of fenpropathrin exposure to greenhouse workers (Tame®) includes residue estimates from cotton and tomato related commodities. The population subgroup considered a reasonable representation of the workforce was the "U.S. Population ages 16 and older". As indicated in the table, the occupation with the highest predicted exposure was harvesters. The estimated average dosage for combined exposures was 30.23 μg/kg body weight /day and the estimated maximum dosage was 45.09 μg/kg body weight /day.

TABLE X: Combined acute occupational and dietary exposure to fenpropathrin from the use of Tame® on greenhouse crops.

	Absorbed Daily Dosage (μg/kg/day)		
Occupational Activity	**Occupational[a]**	**Dietary[b]**	**Combined**
Mixer/Loaders	0.95 (2.15)	0.49	1.44 (2.64)[c]
Applicators	11.48 (31.92)	0.49	11.97 (32.41)[c]
Harvesters	29.74 (44.60)	0.49	30.23 (45.09)

[a] values represent the mean and maximum (in parenthesis).
[b] exposure of U.S. population (16 + years) to cotton related byproducts, tomatoes, and tomato byproducts.
[c] combined values include inhalation exposure of 6 μg/kg/day (based on 50% absorption of the exposure, i.e., 1.2 μg/kg/day).

b) Short-Term Exposure

The average and maximum absorbed daily dosage for short-term exposure, for each occupational activity, was determined by multiplying the potential acute dosage (ADD) (see TABLES III and IV) by the number of exposure days (6 days per week) and dividing by the number of days in the time period (7 days). These values along with the estimate of dietary exposure to potential workers (U.S. population aged 16 years and older) are presented in the TABLES XI and XII. As indicated, the average daily absorbed daily dosages of fenpropathrin from the use of Danitol® ranged from approximately 1 to 21 µg/kg, with the estimated exposure to cotton scouts being the highest. When estimates were based on maximum potential exposure, the values ranged from approximately 2 to 49 µg/kg, with the estimated exposure to cotton scouts being the highest.

TABLE XI: Combined short-term occupational and daily dietary exposure to fenpropathrin from the use of Danitol® on cotton.

	Absorbed Daily Dosage (µg/kg/day)		
Occupational Activity	**Occupational[a]**	**Dietary[b]**	**Combined[a]**
Aerial Application			
Mixer/Loader	4.39 (12.35)	0.49	4.81 (12.81)
Pilots	1.26 (4.33)	0.49	1.68 (4.75)
Flaggers	3.43 (20.57)	0.49	3.85 (20.99)
Ground Application			
Mixer/Loader	0.69 (1.92)	0.49	1.18 (2.41)
Applicators	2.67 (20.75)	0.49	3.09 (21.17)
Cotton Scouts	20.61 (48.93)	0.49	21.03 (49.35)

[a] values presented represent the mean and maximum (in parenthesis) predicted values and were calculated by multiplying the ADD in TABLE III by 6/7.

[b] exposure of U.S. population (16 + years) to cotton related byproducts, tomatoes, and tomato byproducts.

TABLE XII presents the combined values for short-term occupational exposure to Tame® and dietary exposure to Danitol®. As indicated, the average absorbed daily dosages of fenpropathrin from the use of Tame® were approximately 2, 11, and 26 μg/kg/day for mixer/loaders, applicators, and harvesters, respectively. When estimates were based on maximum potential exposure, the values were approximately 2, 28, and 41 μg/kg/day for mixer/loaders, applicators, and harvesters, respectively. Combined fenpropathrin exposures for workers using Tame® included dermal, inhalation, and dietary exposures. The dermal exposure was based on an assumed 32% dermal penetration and the inhalation exposure assumed 50% absorption (exposure was 1.2 μg/kg/day).

TABLE XII: Combined short-term occupational and daily dietary exposure to fenpropathrin from the use of Tame® on greenhouse crops.

	Absorbed Daily Dosage (μg/kg/day)		
Occupational Activity	**Occupational[a]**	**Dietary[b]**	**Combined[a]**
Mixer/Loaders	0.81 (1.33)	0.49	1.90 (2.42)
Applicators	9.84 (26.85)	0.49	10.93 (27.94)
Harvesters	25.49 (38.22)	0.49	25.98 (41.13)

[a] values presented represent the mean and maximum (in parenthesis) predicted values and were calculated by multiplying the ADD in TABLE IV by 6/7.

[b] exposure of U.S. population (16+ years) to cotton related byproducts, tomatoes, and tomato byproducts.

C. RISK CHARACTERIZATION

In order to characterize the potential risks associated with exposure to fenpropathrin, margins of safety (MOSs) were calculated for both occupational and dietary exposures. An MOS for one or more routes of exposure with a single NOEL is defined as the ratio of the NOEL to the total absorbed dosage. For exposures involving multiple routes with different NOELs, the combined margin of safety is defined as the inverse of combined hazard index ($HI_{combined}$) times an overall uncertainty factor (UF). The $HI_{combined}$ is defined as the sum of exposures divided by the reference doses (RfD) for each route. The RfD is the NOEL divided by an UF. For fenpropathrin, the uncertainty factors for each route of exposure were assumed to be the same as the overall uncertainty factor, and, therefore, are considered to be unity for purposes of this calculation.

$$MOS = NOEL \div \text{Absorbed Dosage}$$

$$MOS_{combined} = (HI_{combined})^{-1} \times UF$$

$$HI_{combined} = (Exp_1 \div RfD_1) + (Exp_2 \div RfD_2) + \ldots + (Exp_n \div RfD_n)$$

$$RfD = NOEL \div UF$$

An example of a situation requiring the Hazard Index calculation would be the estimation of a margin of safety for acute occupational exposure to fenpropathrin. This is because two potential routes of exposure exist, i.e., dermal and inhalation, with two different NOELs (32 mg/kg and 6 mg/kg). This is in contrast to short-term exposure where the Hazard Index approach was not used because only one NOEL was used for the MOS calculation. The justification for the MOS calculation method is indicated under the appropriate headings.

1. Occupational Exposure

a) Acute Exposure

For occupational exposures to fenpropathrin from the treatment of cotton with Danitol®, a single route of exposure (dermal) is assumed. Margins of safety were calculated for the average and maximum potential exposures. The NOEL used in estimating these values was 100 mg/kg body weight. This NOEL was based on ataxia, tremors and hypersensitivity observed in a rat dermal toxicity study (see Hazard Identification section). After accounting for dermal absorption (32%), the adjusted acute NOEL was 32 mg/kg body weight. For mixer/loaders involved with the aerial application of Danitol® on cotton, the estimated average and maximum absorbed dosages were 5.12 and 14.4 µg/kg/day, respectively. The margins of safety were, therefore, 6,250 (32,000 ÷ 5.12), and 2,222 (32,000 ÷ 14.4). These values along with margins of safety for other occupational activities were rounded off to two significant digits and presented in TABLE XIII. As indicated, margins of safety, based on average and upper-bound exposure estimates, are greater than 500 for all occupational activities.

TABLE XIII: Estimated margins of safety for acute exposure to fenpropathrin for occupational activities associated with the treatment of cotton with Danitol®.

Occupational Activities	Margin of Safety[a]
Aerial Application	
Mixer/Loaders	6,300 (2,200)
Pilots	20,000 (6,300)
Flaggers	7,700 (1,300)
Ground Application	
Mixer/Loaders	33,000 (14,000)
Applicators	10,000 (1,300)
Cotton Scouts	1,300 (560)

[a] margin of safety for average and maximum exposure (in parenthesis for each occupational activity. All values have been rounded to two significant digits. The margin of safety was defined as the ratio of the NOEL to the absorbed dosage. The adjusted NOEL used for acute exposure to fenpropathrin was 32 mg/kg.

For occupational-related exposure to fenpropathrin from the use of Tame® (greenhouse crops), margins of safety were estimated. Since the total dosage for mixer/loaders and applicators assumes both dermal and inhalation exposure, a combined margin of safety (hazard index method) was estimated. Fenpropathrin exposure to harvesters included dermal exposure only, as inhalation exposure was assumed to be negligible. The margin of safety for this group was determined by taking the ratio of the NOEL to the absorbed dosage. For potential dermal exposure, the NOEL used was 100 mg/kg. After adjusting for dermal absorption (32%), the adjusted NOEL used was 32 mg/kg (32,000 μg/kg/day). The NOEL used for inhalation exposure was assumed to be the same as the acute NOEL for oral exposure, i.e., 6 mg/kg (6,000 μg/kg/day). The following is an example of the calculation for combined margin of safety:

For mixer/loader, maximum dermal exposure estimate was 1 μg/kg/day.
Adjusted for dermal absorption (32%), dermal dosage was 0.32 μg/kg/day.

Inhalation exposure was 1.2 μg/kg/day.
Adjusted for absorption (50%), inhalation dosage was 0.6 μg/kg/day.

$$MOS_{combined} = ((0.32 \div 32{,}000) + (0.6 \div 6{,}000))^{-1} = 9{,}091 \approx 9{,}100$$

Estimated margins of safety for all three occupational activities are presented in TABLE XIV. As indicated in the table, all margins of safety presented are greater than 700.

TABLE XIV: Estimated margins of safety for acute exposure to fenpropathrin for occupational activities associated with the treatment of greenhouse crops with Tame®.

Occupational Activities	Margin of Safety[a]
Mixer/Loaders[b]	9,100 (6,700)
Applicators[b]	2,300 (930)
Harvesters[c]	1,100 (720)

[a] margin of safety for average and maximum exposure (in parenthesis) for each occupational activity. All values have been rounded to two significant digits.

[b] the margin of safety is based on potential dermal and inhalation exposure. Adjusted dermal NOEL used was 32 mg/kg, oral NOEL 6 mg/kg was used for inhalation.

[c] inhalation exposure is assumed to be negligible.

b) Short-Term (1-3 weeks) Exposure

Since it is not possible to exclude the dietary component of worker exposure to fenpropathrin, margins of safety for only short-term occupational exposure were not calculated. The combined short term occupational and dietary exposures are presented in TABLE XVIII.

2. Dietary Exposure

a) Acute (Daily) Exposure

Margins of safety for potential acute dietary exposure to fenpropathrin were calculated by taking the ratio of the experimentally determined NOEL (i.e., 6 mg/kg body weight, based on convulsions, ataxia, tremors, and death observed within the first week in a rat developmental study) to the potential dietary dosage . The values presented in TABLE XV reflect the potential dietary dosage of fenpropathrin from cotton and tomato related commodities. As indicated, all values are greater than 4,000.

TABLE XV: Margins of safety (MOS) for potential acute dietary exposure to fenpropathrin from consumption of cotton and tomato related commodities.

Population Sub-group	MOS
U.S. Population	8,200
Western Region - U.S. Population	7,800
Nursing Infants (<1 year)	17,000
Non-Nursing Infants (<1 year)	5,100
Females (13+/P[a]/NN[b])	12,000
Females (13+N[c])	13,000
Children (1-6 years)	4,600
Children (7-12 years)	6,600
Males (13-19 years)	8,900
Females (13-19 years/NP[d]/NN)	11,000
Males (20+ years)	12,000
Females (20+/NP/NN)	14,000
Seniors (55+ years)	14,000
U.S. Population (16+ years)	12,000

a = pregnant
b = not nursing
c = nursing
d = not pregnant
e = Exposure is evaluated as a function of user-days (i.e., day which at least one commodity, containing fenpropathrin is consumed).
f = Values represent the 95th percentile of consumer-day exposure.
NOTE: All values have been rounded to 2 significant digits.

b) Short-Term (1-3 weeks) Exposure

Margins of safety for potential short-term dietary exposure to fenpropathrin were calculated by taking the ratio of the experimentally determined NOEL (i.e., 3 mg/kg body weight, based on tremors and death observed in the second week of a chronic feeding study in dogs) to the potential dietary dosage. Since the only difference between acute and short-term exposures is the NOEL (acute NOEL is 6 mg/kg), the estimated margins of safety for short-term exposure are a factor of two less than the acute values. All margins of safety for short-term dietary exposure to fenpropathrin are, therefore, greater than 2,000.

3. Combined (Occupational and Dietary) Exposure

a) Acute (daily) Exposure

Since agricultural workers are assumed to have the same potential for dietary exposure to pesticides as the general public, their total potential exposure should incorporate both occupational and dietary exposure considerations. The dietary component of exposure was based on potential exposure to the U.S. population 16 years of age and older. Margins of safety for exposure to Danitol® and Tame® were, therefore, calculated using the previously described hazard index method. For example, the calculation for aerial application mixer/loaders was as follows: The potential exposure was 5.12 µg/kg. The NOEL for dermal exposure was 32 mg/kg. The calculated potential dietary exposure was 0.49 µg/kg, and the oral NOEL for acute exposure was 6 mg/kg. The margin of safety, therefore, was 4,100.

$$MOS_{(combined)} = ((5.12 \div 32{,}000) + (0.49 \div 6{,}000))^{-1} = 4138$$

$$= 4{,}100 \text{ (rounded to two significant digits)}$$

TABLE XVI presents the estimated margins of safety for average and maximum acute fenpropathrin exposure for the various occupational activities involved with the use of Danitol® (note that exposure is for occupation and dietary). All estimates are greater than 500.

Table XVI: Margins of safety for acute potential occupational exposure to fenpropathrin from Danitol® treatment of cotton and dietary exposure from cotton related commodities and tomatoes.

Occupational Activities	Margin of Safety[a]
Aerial Application	
Mixer/Loaders	4,100 (1,900)
Pilots	7,800 (4,200)
Flaggers	4,800 (1,200)
Ground Application	
Mixer/Loaders	9,400 (6,600)
Applicators	5,600 (1,200)
Cotton Scouts	1,200 (540)

[a] average and maximum exposure (in parenthesis) for each occupational activity. All values have been rounded to two significant digits.

As previously indicated, occupational exposure to fenpropathrin through the use of Tame® on greenhouse crops potentially involves dermal as well as inhalation exposure. Furthermore, as was the case with the use of Danitol® on cotton, potential dietary exposure of workers using Tame® was included. TABLE XVII presents the estimated margins of safety for workers involved in various occupational activities relating to the use of Tame®. Exposure estimates for mixer/loaders and applicators included dermal, inhalation, and dietary. Exposure estimates for harvesters included dermal and dietary only as inhalation was assumed to be negligible. The NOELs used were: 32 mg/kg for dermal, and 6 mg/kg for inhalation and dietary exposures. The calculations were based on the combined MOS (hazard index) as previously described. For example, the calculation for applicators based on average exposure was as follows: The dermal dosage was 10.88 µg/kg. The estimated inhalation dosage was 0.6 µg/kg. The calculated potential dietary exposure was 0.49 µg/kg. The NOEL used for both dietary and inhalation was 6 mg/kg. The margin of safety is, therefore;

$$MOS_{(combined)} = ((10.88 \div 32{,}000) + (0.6 \div 6{,}000) + (0.49 \div 6{,}000))^{-1}$$
$$\approx 1900$$

As indicated in the table, all margins of safety were greater than 600.

TABLE XVII: Margins of safety for potential acute occupational exposure to fenpropathrin from Tame® treatment of greenhouse crops and acute dietary exposure from cotton and tomato related commodities.

Occupational Activities	Margin of Safety[a]
Mixer/Loaders	5,200 (4,300)
Applicators	1,900 (860)
Harvesters	990 (680)

[a] average and maximum exposure (in parenthesis) for each occupational activity. All values in this table have been rounded to two significant digits.

b) Short-Term (1-3 weeks) Exposure

Margins of safety for short-term exposure, i.e., one to three weeks, to workers using Danitol® included both dermal and dietary exposures. Based on the toxicology profile, the NOEL for clinical signs at time periods greater than 1 week was 3 mg/kg/day (based on tremors and death observed in the second week of a chronic feeding study with dogs). NOELs based on short-term dermal, inhalation, or dietary exposures were not available. Margins of safety, therefore, were based on the ratio of the oral NOEL (3 mg/kg/day) to the total absorbed dosage. The dietary exposure component was assumed to be the same as that used for acute exposure. The margins of safety based on average and maximum exposure estimates are presented in TABLE XVIII. As indicated in TABLE XVIII, margins of safety based on average exposure ranged from 140 to 2,500. The occupation with the lowest margin of safety is cotton scouts. All other occupations had margins of safety greater than 600. Margins of safety for based on maximum potential exposure ranged from 61 to 1,200. The occupation with the lowest margin of safety was cotton scouts.

TABLE XVIII: Margins of safety for short-term occupational exposure to fenpropathrin from Danitol® treatment of cotton and acute dietary exposure from cotton related commodities and tomatoes.

Occupational Activities	Margin of Safety[a]
Aerial Application	
Mixer/Loaders	620 (230)
Pilots	1,800 (630)
Flaggers	780 (140)
Ground Application	
Mixer/Loaders	2,500 (1,200)
Applicators	970 (140)
Cotton Scouts	140 (61)

[a] the margin of safety was based on a dermal and dietary exposure. The NOEL used was 3 mg/kg/day.

[b] average and maximum exposure (in parenthesis) for each occupational activity, all values have been rounded to two significant digits.

Margins of safety for short-term exposure to workers exposed to Tame® are presented in TABLE XIX. The values are based on average and maximum exposure estimates. The values include dermal, inhalation and dietary exposures for all occupational activities except harvesters. Harvesters were assumed to have negligible inhalation exposure. As previously discussed for short-term exposure with Danitol®, the NOEL used was 3 mg/kg/day all routes of exposure. As indicated in the table, margins of safety based on average exposure ranged from 120 to 1,600, with harvesters exhibiting the lowest value. Margins of safety based on potential maximum daily exposure ranged from 73 to 1,200, with harvesters exhibiting the lowest value.

Table XIX: Margins of safety for potential short-term occupational exposure to fenpropathrin from Tame® treatment of greenhouse crops and acute dietary exposure from cotton and tomato related commodities.

Occupational Activities	Margin of Safety[a]
Mixer/Loaders	1,600 (1,200)
Applicators	270 (110)
Harvesters	120 (73)

[a] margins of safety was based on a dermal, inhalation, and dietary exposure. All values in this table have been rounded to two significant digits. Average and maximum exposure (in parenthesis) are presented.

V. RISK APPRAISAL

A health risk assessment was conducted for the potential exposure of fenpropathrin to agricultural workers and the general public from dietary sources (cotton byproducts and tomatoes). The routes of exposure considered were dermal and inhalation for occupational and oral for dietary, under acute and short-term conditions. Risk assessment is the process used to evaluate the potential for human exposure to a substance and the likelihood that the potential exposure will cause adverse health effects in humans under specific exposure conditions. Every risk assessment has inherent limitations on the application of existing data to the prediction of potential risk to the human population. This makes it necessary for certain assumptions and extrapolations to be incorporated into the hazard identification, dose-response assessment, and exposure assessment processes. This, in turn, results in a level of uncertainty in the risk characterization. Qualitatively, risk assessments for all chemicals have similar uncertainties. The degree or magnitude of the uncertainty, however, can vary depending on the availability and quality of the data, and the types of exposure scenarios being assessed. One of the primary assumptions, which is inherent in all risk assessments using animal data is that effects observed in rodents represent expected effects in humans at comparable dosages. In the absence of actual human data, this assumption and resulting extrapolation are necessary. Areas of uncertainty specific to this risk assessment are delineated in the following discussion.

In the dietary assessment, since neither table top nor market basket data were available, residue estimates were based on field trials and tolerance values. These field studies were conducted to establish tolerances for specific raw agricultural commodities and, therefore, were designed to obtain the highest potential residue under the conditions indicated on the product label. When field study data were inadequate or non-existent, residue values were assumed at tolerance levels. The resulting estimate of exposure was likely an overestimate of actual exposure from dietary sources. Furthermore, it was assumed that residue levels were stable; i.e., residue values do not change over time, the concentration does not decrease when the commodity is washed, the residue concentration is not reduced by processing of the commodity, and all consumed commodities contain the highest reported residue.

For occupational exposure, surrogate data were used for dosage calculations. Since actual exposure data were not available, the dermal exposures were based on exposure rates for other pesticides. Based on vapor pressure and surrogate data, the inhalation exposure was assumed to be negligible. While the values used were considered the best available information, uncertainties are inherent whenever extrapolation from surrogate data are used to characterize potential risk.

In addition to the dermal and inhalation routes from occupational exposure, dietary exposure was evaluated in order to estimate a combined potential exposure for the various occupational activities. The dietary component was based on a national consumption survey conducted by the U.S. Department of Agriculture. The exposure data used in the dietary assessment of workers was restricted to those survey respondents age 16 years and older. This assumes that the number of workers under this age are too small to influence the interpretation of the analysis. Furthermore, inherent in the use of the national survey is the assumption that the result is representative of California residents. For cotton and tomato byproducts, this assumption may be reasonable. For other commodities, this assumption may not be totally valid in light of the ethnic diversity in the state.

In calculating the margins of safety for exposure to fenpropathrin from the use of Danitol® on cotton, a NOEL of 100 mg/kg/day was used for acute dermal exposure. This NOEL was based on clinical signs observed in dermal toxicity studies with rats and mice. The clinical signs reported in the study included ataxia, tremors, and hypersensitivity. After adjusting for dermal penetration, the adjusted NOEL was 32 mg/kg/day.

For acute dietary and inhalation exposure a NOEL of 6 mg/kg was established from a rat developmental study. The clinical signs reported included death, convulsions, ataxia, and tremors. These signs occurred between days one and seven of the study. Furthermore, a NOEL of 3 mg/kg/day was reported in a dog feeding study. The clinical observations included tremors, ataxia, and languidity. All reported within two weeks of the study initiation. Inasmuch as occupational activities involved with the use of fenpropathrin products may result in multiple exposures as workers move from field to field, this NOEL was utilized in estimating margins of safety for short-term multiple exposures.

While addressing occupational exposure to fenpropathrin from the use of Tame® on greenhouse crops, dermal exposure was assumed to be the primary route. In contrast to the analysis with Danitol® use on cotton, potential inhalation exposure was considered for mixer/loaders and applicators. Unlike mixer/loaders and applicators, inhalation exposure is assumed to be insignificant for greenhouse harvesters as these workers should not be exposed to pesticide spray or dust. The NOELs used in calculating the margins of safety were the same as with Danitol®, i.e., 32 mg/kg for acute dermal exposure, 6 mg/kg for acute dietary and inhalation exposure, and 3 mg/kg for short-term exposure.

In general, a margin of safety equal to or greater than 100 is considered adequate for the protection of human health when it is based on NOELs from non-human mammalian studies. When the potential toxicity is considered severe (e.g., tremors and death), a larger margin of safety may be warranted. Margins of safety based on maximum exposure, for multiple exposure scenarios, may not be representative of actual exposures. Based on the data base reported in this document, margins of safety for both mean and maximum acute exposures to fenpropathrin from occupational and dietary use of Danitol® and Tame®, are in excess of 500 for agricultural workers. Margins of safety for acute dietary exposure to the general population, i.e., those not exposed occupationally, were also estimated. On the basis of the 95th percentile of exposure to fenpropathrin from cotton and tomato related commodities, all values were in excess of 2,000. Margins of safety for short-term occupational exposure associated with Danitol® and Tame® use were all greater than 100 when considering average exposures. With the use of Danitol® on cotton, all margins of safety based on maximum exposure were greater than 100 except for cotton scouts. The estimated margin of safety for short-term exposure to cotton scouts was 61. With the use of Tame® on greenhouse crops, all margins of safety, based on maximum exposure, were greater than 100 except for harvesters. The estimated margin of safety for short-term exposure to harvesters was 78. Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures, may be an unrealistic estimate.

VI. TOLERANCE ASSESSMENT

A. BACKGROUND

A tolerance is the maximum, legal amount of a pesticide residue that is allowed on a raw or processed agricultural commodity, or in an animal tissue used for human consumption. The U.S. EPA tolerance program was developed as an enforcement mechanism to identify illegal residue concentrations resulting from potential non-compliance with the product label requirements (e.g., improper application rates or methods, inadequate pre-harvest intervals, direct or indirect application to non-approved commodities). Tolerances are enforced by the Food and Drug Administration (FDA), the U.S. Department of Agriculture (USDA), and state enforcement agencies (e.g., Pesticide Enforcement Branch of DPR).

Current pesticide tolerances are generally set at levels that are not expected to produce deleterious health effects in humans from chronic dietary exposure. The data requirements for establishing a specific tolerance include: 1) toxicology data for the parent compound, major metabolites, degradation products and impurities, 2) product chemistry, 3) analytical methods(s) that are readily available, accurate and precise, 4) measured residues in crops used for animal feeds, 5) measured residues in animal tissues (e.g., meat, milk, and eggs) from direct or indirect (feed) applications, 6) measured residue levels from field studies. The minimum requirements for the field study include: 1) an application rate at or above the highest rate on the product label, 2) the greatest number of allowable repeat applications, 3) the shortest pre harvest interval listed on the product label. Generally, the registrant of the pesticide requests a commodity-specific tolerance, which is equal to the highest measured residue, or some multiple of that value, from the field trial using the specific pesticide.

Assembly Bill 2161 (Bronzan and Jones, 1989) requires the DPR to "conduct an assessment of dietary risks associated with the consumption of produce and processed food treated with pesticides." In the situation where "any pesticide use represents a dietary risk that is deleterious to the health of humans, the DPR shall prohibit or take action to modify that use or modify the tolerance" As part of the tolerance assessment, a theoretical dietary exposure for a specific commodity and specific population sub-groups can be calculated from the product of the tolerance and the daily consumption rate.

B. ACUTE EXPOSURE

An acute exposure assessment using the residue level equal to the tolerance is conducted for each individual label-approved commodity. The TAS Exposure-4™ software program and the USDA consumption data base are used in the assessment. The acute tolerance assessment does not routinely address multiple commodities at tolerance levels because the probability of consuming multiple commodities that are all at the tolerance level significantly decreases as the number of commodities included in the assessment increases.

A dietary exposure assessment for fenpropathrin exposure was conducted using tolerance levels as assumed residue values. TABLE XVI presents the calculated margin of safety (MOS) range for each label approved commodity. The range is based on the various population sub-groups (see exposure section for identification of population sub-groups. As indicated, all margins of safety are greater than 400.

TABLE XVI: Fenpropathrin tolerances and corresponding margins of safety (MOSs) for potential acute dietary exposure.

Commodity	Tolerance (ppm)	Margins of Safety[a] low	Margins of Safety[a] high
Cottonseed	0.02	4,700	12,000
Cottonseed oil	0.02	1,600	4,000
Cattle meat	0.02	12,000	27,000
Cattle fat	0.02	52,000	1600,000
Cattle meat byproduct	0.02	110,000	1,000,000
Eggs	0.02	12,000	51,000
Milk	0.03	440	3,300
Poultry meat	0.02	9,500	31,000
Poultry fat	0.02	73,000	300,000
Poultry meat byproduct	0.02	930,000	>1,000,000

[a] Margins of safety are defined as the ratio of the NOEL to the absorbed dosage.

C. CHRONIC EXPOSURE

A chronic exposure assessment using residues equal to the established tolerances for individual or combinations or commodities has not been conducted because it is highly improbable, if not impossible, that an individual would chronically consume single or multiple commodities with pesticide residues at the tolerance levels. Support for this conclusion comes from CDFA pesticide monitoring programs that indicate that less than one percent of all sampled commodities have residue levels at or above the established tolerance (CDFA, 1990).

VII. CONCLUSIONS

The toxicology data base for fenpropathrin has indicated potential adverse effects in animal studies. These effects are generally associated with neurotoxicity and appear to be primarily a response to acute exposure. No clear indication of chronic toxicity, oncogenicity, or developmental toxicity was demonstrated. Studies did indicate that this pesticide may have mutagenic potential in bacteria and in mammalian cells grown *in vitro*. Based on the current data base, all margins of safety for acute occupational and dietary exposure to fenpropathrin from Danitol® (proposed for use on cotton), and Tame® (proposed for use on greenhouse crops), are greater than 100. For short-term exposures, all margins of safety greater than 100 except those for cotton scouts and greenhouse harvesters when estimates were based on maximum potential exposure (*the values for harvesters involved with the use of Tame® assumed a label modification that requires the use of gauntlet gloves. Without this modification, exposure would be significantly increased for this occupation*). Since it is considered unlikely that an individual worker would be exposed to the maximum potential pesticide dosage each period of a multiple exposure scenario, margins of safety based on maximum exposure, for short-term exposures, may be an unrealistic estimate. In general, a margin of safety equal to or greater than 100 is considered adequate for the protection of human health when it is based on NOELs from non-human mammalian studies. When the potential toxicity is considered severe (e.g., tremors and death), a larger margin of safety may be warranted.

An additional dietary assessment of acute risk potential, based on residue levels set at U.S. EPA tolerances, indicated that little potential exists for adverse health effects from dietary exposure to fenpropathrin.

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APPENDIX A

Toxicology Summary Sheets

TO: James Herota, Registration Specialist
Pesticide Registration Branch

FROM: Medical Toxicology Branch

Date: 10/21/92 (original)
5/6/93 (revised)

PRODUCT REGISTRATION RECOMMENDATION SHEET

Formulated Product Name: DANITOL 2.4 EC Spray (Tame 2.4 EC Spray)
Chemical Code #: 2234 **ID #:** 138381N
EPA Reg. #: 59639-35 **SB 950 #:** New A.I.
Document #: 50489-003, -006 to -010, -014, -037 to -047, -049 to -073, -090, and -096 to -097
Company Name: VALENT USA Corporation

RECOMMENDATION:

Submitted as as new active ingredient Section 3 registration request.

The data are adequate to make a complete toxicological evaluation of the subject product.

Product label identifies all potential hazards indicated by the data reviewed.

Decision regarding registration will be deferred until the SB950 Adverse Effects Advisory Panel completes its risk assessment prioritization.

Peter Leung
Peter Leung, Ph.D.
Staff Toxicologist

5/6/93
Date

G Patterson
Gary Patterson, Ph.D.
Senior Toxicologist

5/7/93
Date

J Gee
Joyce Gee, Ph.D.
Senior Toxicologist

5/7/93
Date

TO--File: Registration **Registration Specialist:** James Herota
Branch: Registration
FROM--Medical Toxicology

DATA PACKAGE SUMMARY AND RECOMMENDATION SHEET

Active Ingredient: Fenpropathrin
Formulated Product Name: DANITOL 2.4 EC Spray
Formulation: Fenpropathrin = 30%, Inerts = 70%
Chemical Code #: 2234 **ID #:** 138381N
EPA Reg. #: 59639-35 **SB 950 #:** New A.I.
Document #: 50489-003, -006 to -010, -014, -037 to -047, -049 to -073, -090, and -096 to -097
Company Name: VALENT USA Corporation

SUMMARY: ("CDFA One-liners" from each study worksheet, significant information not mentioned in worksheets, other pertinent information for ongoing review or registration. Attach additional sheets if needed)

Danitol 2.4 EC Spray was transferred to Valent U.S.A. Corp. on March 23, 1992 and assigned EPA Reg. # 59639-77. Subsequently, the file name for this registration has been changed to Tame 2.4 EC Spray.

Toxicology data for Danitol 2.4 EC (Formulation CC-17228) and the active ingredient, fenpropathrin, were submitted to support a Section 3 Registration request for controlling insects including beet armyworm, pink bollworm and sweet potato whitefly on cotton crop.

Fenpropathrin has also been referred to as S-3206, WL-41707, and SD-41706.

ACUTE STUDIES - Technical

	Toxicity Category
Acute Oral Toxicity LD_{50}	I
Acute Dermal Toxicity LD_{50}	II
Acute Inhalation Toxicity LC_{50}	Not submitted and not required at this time *
Primary Eye Irritation	III
Primary Dermal Irritation	Unacceptable but possibly upgradeable *

* See Conclusions

Acute Oral Toxicity
007 9838, "Acute Oral Toxicity of S-3206 (91.8%) in Rats", (Sumitomo Chemical Company, Ltd., Laboratory of Biochemistry and Toxicology, Hyogo, Japan, Lab Report No. FT-30-0081, 1/17/83); 811; S-3206 Technical Grade, Lot No. 2TC019 (purity = 91.8%), dissolved in corn oil and dosed at 10 ml dosing mixture/kg; 0 (vehicle), 10, 25, 50, 60, 72, 86, 104, 125 mg/kg; 10 animals/sex/dose level; Mortality- male: 0/10, 0/10, 1/10, 2/10, 4/10, 6/10, 7/10, 9/10, 10/10, female: 0/10, 0/10, 0/10, 3/10, 6/10, 6/10, 6/10, 9/10, 10/10; Clinical Observations- muscular fibrillation, diarrhea, tremors, ataxia, decreased spontaneous activity; limb paralysis, irregular respiration, salivation, urinary incontinence; Necropsy- black-brownish point on stomach, white substance in urinary bladder, uterus distended with fluid, incrustation on skin, considered not compound-related; LD50 (M) = 70.6 (53.7-92.7), (F) = 66.7 (50.6-87.9) mg/kg; **NOEL = 10 mg/kg; Toxicity Category II; **Acceptable.** (Duncan, 10/25/90)

037 91117, "Acute Oral Toxicity of S-3206 in Rats", (Sumitomo Chemical Company, Ltd., Laboratory of Biochemistry and Toxicology, Hyogo, Japan, Lab Report No. FT-20-0076, 7/28/82); 811; S-3206, Lot No. T-1 (purity = 97.3%), suspended in 10% gum arabic and dosed at a volume of 20 ml dosing suspension/kg; 0 (vehicle), 25, 50, 90, 120, 160, 220, 300 mg/kg; 10 animals/sex/dose level; Mortality- male: 0/10, 0/10, 0/10, 2/10, 0/10, 6/10, 5/10, 9/10, female: 0/10, 0/10, 0/10, 5/10, 6/10, 8/10, 10/10, 10/10; Clinical Observations- muscular fibrillation, tremors, ataxia, limb paralysis, loss of righting reflex, hyperpnea, dyspnea, irregular respiration, lacrimation, salivation, urinary incontinence, diarrhea, hyperexcitability; Necropsy- no compound-related changes; LD50 (M) = 164 (115-234), (F) = 107 (69.8-164) mg/kg; **NOEL = 25 mg/kg; Toxicity Category II; **Acceptable.** (Duncan, 10/23/90)

039 91119, "Acute Oral Toxicity of S-3206 in Rabbits", (Sumitomo Chemical Company, Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-00-0039, 9/80); 811; S-3206, Lot No. 90403 (purity = 96.2%), dosed as a mixture in corn oil at a volume of 2-4 ml dosing mixture/kg; 0 (vehicle), 89, 133, 200, 300, 450, 675, 1000 mg/kg; 5 animals/sex/dose level; Mortality- male: 0/5, 0/5, 0/5, 0/5, 0/5, 1/5, 3/5, 4/5, female: 0/5, 0/5, 0/5, 0/5, 1/5, 3/5, 3/5, 4/5; Clinical Observations- muscular fibrillation, tremor, whole body ataxia, slow respiration, diarrhea; Necropsy- nothing remarkable; LD50 (M) = 675 (504-905), (F) = 510 (300-867) mg/kg; **NOEL = 89 mg/kg; Toxicity Category III; **Acceptable** (Duncan, 10/12/90)

006 9830, "Acute Oral Toxicity of S-3206 Technical in Mice", (Sumitomo Chemical Company, Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-50-0035, 8/80); S-3206, Lot No. 022018 (purity = 97.0%), dosed as a mixture in corn oil at a volume of 10 ml dosing mixture/kg; 30, 45, 67, 100 mg/kg; 10 animals/sex/dose level; Mortality- male: 0/10, 1/10, 5/10, 9/10, female: 0/10, 3/10, 7/10, 9/10; Clinical Observations- tremor, clonic convulsion, hind limb or whole body ataxia; Necropsy- no particular changes; LD50 (M) = 67 (49.3-91.2), (F) = 58 (44.3-76.0) mg/kg; **NOEL = 30 mg/kg; Toxicity Category II; **Acceptable.** (Duncan, 10/12/90)

006 9832, "Acute Oral Toxicity of S-3206 in Rats", (Institute for Biological Science, Hyogo, Japan, Lab Report No. FT-50-0018, 1/79); S-3206, Lot No. 022018 (purity = 97.0%), dosed as a mixture in corn oil at a volume of 5 ml dosing mixture/kg; 15, 20, 30, 50, 59, 77, 100, 130 (10 animals/sex/dose level), and 169 (10M) mg/kg; Mortality- male: 0/10, 0/10, 0/10, 5/10, 4/10, 9/10, 9/10, 10/10, 10/10, female: 0/10, 0/10, 2/10, 5/10, 7/10, 9/10, 9/10, 10/10; Clinical Observations- decrease of spontaneous motor activity, hypersensitivity, fibrillation, tremor, clonic convulsion, salivation, lacrimation, urinary incontinence, hind limb ataxia; Necropsy- no particular changes; LD50 (M) = 54.0 (43.5-67.0), (F) = 48.5 (37.6-62.6) mg/kg; **NOEL = 15 mg/kg; Toxicity Category I; **Acceptable.** (Duncan, 10/12/90)

Hazard category I for the acute oral toxicity has been chosen. This is based on an acute oral toxicity study performed in rats (Document 50489-001, DPR record number 9832).

Acute Dermal Toxicity

006 9823, "Acute Dermal Toxicity (LD50) Study in Rabbits", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-002, 10/26/81); S-3206 Technical Grade, moistened with physiological saline; 0 (untreated) (1M/1F), 2000 (5M/5F) mg/kg; abraded skin, occlusive wrap, 24-hour exposure; no mortality; Clinical Observations- soft stool, nasal discharge; erythema and edema at application site; Necropsy- no test-article effects; Histopathology- no test-article effects; LD50 (M and F) > 2000 mg/kg; Toxicity Category III; **Acceptable. (Duncan, 10/15/90)

006 9819, "Acute Dermal Toxicity of S-3206 Technical in Mice", (Sumitomo Chemical Company, Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-60-0036, 8/80); 812; S-3206, Lot No. 022018 (purity = 97.0%), applied as a mixture in corn oil (concentration and dosing volume not reported); occlusive wrap, 24-hour exposure; 100, 300, 600, 1000, 1750, 2500, 5000 mg/kg; 10 animals/sex/dose level; Mortality- male: 0/10, 0/10, 3/10, 8/10, 10/10, 10/10, 10/10, female: 0/10, 0/10, 2/10, 5/10, 9/10, 10/10, 10/10; Clinical Observations- hypersensitivity, tremor, urinary incontinence, hind limb ataxia; Necropsy- no remarkable findings; LD50 (M) = 740 (587-932), (F) = 920 (676-1251) mg/kg, NOEL (M and F) = 100 mg/kg (reported); Toxicity Category II; **Acceptable. (Duncan, 10/16/90)

006 9820, "Acute Dermal Toxicity of S-3206 in Rats", (Institute for Biological Science, Hyogo, Japan, Lab Report No. FT-60-0019, 1/79); 812; S-3206, Lot No. 022018 (purity = 97.0%), dosed as a mixture in corn oil at a volume of 5 ml dosing mixture/kg; 100, 250, 500, 750, 1000, 2500, 5000 mg/kg; 10 animals/sex/dose level; occlusive wrap, 24-hour exposure; Mortality- male: 0/10, 0/10, 0/10, 0/10, 2/10, 8/10, 10/10, female: 0/10, 0/10, 1/10, 3/10, 7/10, 10/10, 10/10; Clinical Observations- hypersensitivity, tremor, urinary incontinence, hind limb ataxia; Necropsy- no remarkable findings; LD50 (M) = 1600 (1150-2220), (F) = 870 (670-1120) mg/kg (reported); reported **NOEL = 100 mg/kg; Toxicity Category II; **Acceptable.** (Duncan, 10/15/90)

Acute Inhalation Toxicity

None submitted and not required at this time because the test article has a low melting temperature and can not be milled to produce an inhalable aerosol.

Primary Eye Irritation

006 9818, "Primary Eye and Skin Irritation Tests of S-3206 in Rabbits", (Institute for Biological Science, Hyogo, Japan, Lab Report No. FT-80-0023, 1/79); 814 - Primary Eye Irritation; S-3206, Lot No. AM-212 (purity = 90.2%), dosed neat; 0.1 ml/eye; 6 animals unwashed, 3 animals washed after 30 sec; examined at 24, 48, 72, 96 h, and 7 d (termination) after treatment; UNWASHED- conjunctivitis only (max. weighted score = 4) which cleared by 72 h; WASHED- conjunctivitis only (max. weighted score = 2) which cleared by 48 h; Toxicity Category III; **Acceptable. (Duncan, 10/16/90)

Primary Dermal Irritation

006 9818, "Primary Eye and Skin Irritation Tests of S-3206 in Rabbits", (Institute for Biological Science, Hyogo, Japan, Lab Report No. FT-80-0023, 1/79); 815 - Primary Dermal Irritation; S-3206, Lot No. AM-212 (purity = 90.2%), applied neat; 0.5 ml/site; one abraded, one intact site/animal, 6 animals; 24-h exposure, occlusive wrap; examined 24, 72 h, and 1 wk (termination) after application; INTACT- no irritation; ABRADED- no irritation; Toxicity Category not determined; **Unacceptable**, but possibly upgradeable with submission of additional data verifying whether the test material is a liquid prior to skin application. (Duncan, 10/16/90)

SUPPLEMENTAL STUDIES

006 9825, "Intravenous Toxicity of SD 41706 (1-24-0-0) in the Mouse", (Summitt, L. M. and Albert, J. R., laboratory not reported, document not dated); SD 41706 (1-24-0-0) (purity not reported), IV infusion over 15 sec as a mixture in glycerol formal at a volume of 1 ml dosing mixture/kg; 0, 1.0, 1.8, 2.4, 3.2, 4.4, 5.6, 7.8 mg/kg (10 males/dose level), and 10.0 mg/kg (20 males); Mortality- 0/10, 0/10, 0/10, 1/10, 0/10, 6/10, 8/10, 8/10, 20/20; Clinical Observations- vocalization, ears flattened, enophthalmos, tremors, clonic convulsions, forelimb flexor-extensor fibrillation; no signs of toxicity reported at 1.0 mg/kg; LD50 (males) = 4.5 (3.9-5.3) mg/kg; **Supplemental.** (Duncan, 10/30/90)

006 9824, "Acute Subcutaneous and Intraperitoneal Toxicity of S-3206 Technical in Rats and Mice", (Sumitomo Chemical Company, Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-60-0037, 8/80); S-3206, Lot No. 022108 (purity = 97.0%), dosed as a mixture in corn oil at a volume of 5-10 ml (rats) or 10-20 ml (mice) dosing mixture/kg; SUBCUTANEOUS/RAT- 250, 500, 750, 1000, 1500, 2000, 2500 mg/kg; 10 animals/sex/dose level; LD50 (M) = 1410, (F) = 900 mg/kg; SUBCUTANEOUS/MOUSE- 100, 150, 200, 250, 375, 500, 750, 1000, 1500, 2000, 4000 mg/kg; 10 animals/sex/dose level; LD50 (M) = 1350, (F) = 900 mg/kg; Clinical Observations (no species differences)- decreased spontaneous activity, deep respiration, hyperexcitability, tremors, salivation, lacrimation, urinary incontinence, limb and whole body ataxia; INTRAPERITONEAL/RAT- 50, 100, 130, 170, 220, 300, 500 mg/kg; 10 animals/sex/dose level; LD50 (M) = 225, (F) = 180 mg/kg; INTRAPERITONEAL/MOUSE- 10, 50, 100, 130, 170, 220, 290, 380, 500 mg/kg; 10 animals/sex/dose level; LD50 (M) = 230, (F) = 210 mg/kg; Clinical Observations (no species differences)- decreased spontaneous activity, muscular fibrillation, tremors, salivation, lacrimation, urinary incontinence, limb and whole body ataxia; Necropsy- formation of granulation tissues in animals dosed subcutaneously; **Supplemental.** (Duncan, 10/12/90)

042 91122, "The Acute Vapor Inhalation Toxicity of DANITOL Technical (SX-1713) in Mice and Rats", (Chevron Environmental Health Center, Richmond, CA, Lab Study No. 2545, 12/15/88); Danitol Technical, Code No. SX-1713 (94.5% fenpropathrin), warmed to 58-60°C to generate vapor (test article has a low melting point and cannot be milled to produce an inhalable aerosol); 0 (air), 0.009 ug fenpropathrin/l (analytical); vapor inhalation, 4-h, whole body exposure; 5 rats, 5 mice/sex/dose level; particle size not reported; no mortality; Clinical Observations- no signs of toxicity; Necropsy- no abnormalities; Histopathology- eosinophilic and lymphocytic infiltration in lung, considered not compound-related; **Supplemental.** (Duncan, 10/24/90)

ACUTE STUDIES - S-3206 2.4 lb/G EC

	Toxicity Category
Acute Oral Toxicity LD_{50}	II
Acute Dermal Toxicity LD_{50}	III
Acute Inhalation Toxicity LC_{50}	III
Primary Eye Irritation	Unacceptable and not upgradeable*
Primary Dermal Irritation	III

* See Conclusions

Acute Oral Toxicity

006, 038; 9831, 91118, "Acute Oral (LD50) Toxicity Study in Rats", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-003, 10/26/81); 811; S-3206 2.4 lb/G EC, dosed as an aqueous emulsion; 25, 40, 64, 81, 102 mg/kg; 5 animals/sex/dose level; Mortality- male: 0/5, 0/5, 0/5, 3/5, 5/5, female: 0/5, 1/5, 1/5, 2/5, 5/5; Clinical Observations- ataxia, tremors, and clonic convulsions occurred in all dose groups; Necropsy- kidney pelvis dilated, lungs congested, lymph node congested, gastric mucosa hyperemic, all considered not test-article related; LD50 (M) = 72.4 (62.1-84.3) mg/kg, (F) = 71.8 (56.1-92.0) mg/kg, (M and F) = 72.1 (63.0-82.5) mg/kg; Toxicity Category II; **Acceptable. (Duncan, 10/12/90)

007 9805, "Acute Oral Toxicity of S-3206 10% EC in Mice", (Institute for Biological Science, Hyogo, Japan, Lab Report No. FT-80-0020, 1/79); 811; S-3206 10% EC, Lot No. 48937 (formulation described in this report), dosed as an aqueous suspension at a volume of 20 ml suspension/kg; 100, 130, 170, 220, 285 mg/kg; 10 animals/sex/dose level; Mortality- male: 0/10, 1/10, 7/10, 9/10, 10/10, female: 0/10, 1/10, 5/10, 10/10, 10/10; Clinical Observations- decreased spontaneous activity, muscular fibrillation, tremor, salivation, urinary incontinence, hypersensitivity, lacrimation, rapid and/or irregular respiration, dyspnea, reduced appetite, hind limb ataxia, loss of righting reflex; Necropsy- no remarkable changes; LD50 (M) = 162 (144-182), (F) = 164 (148-182) mg/kg; **reported NOEL = 100 mg/kg; Toxicity Category II; **Acceptable.** (Duncan, 10/15/90)

Acute Dermal Toxicity

040 91120, "Acute Dermal Toxicity (LD50) Study in Rabbits", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-004, 10/26/81); 812; S-3206 2.4 lb/G EC, applied neat; 0 (untreated) (1M/1F), 2000 (5M/5F) mg/kg; abraded skin, occlusive wrap, 24-hour exposure; no mortality; Clinical Observations- erythema, edema, atonia, coriaceousness, fissuring, desquamation at application site; Histopathology- mild inflammation of skin (hyperkeratosis, infiltration of inflammatory cells in dermis) at application site; LD50 (M and F) > 2000 mg/kg; Toxicity Category III; **Acceptable. (Duncan, 10/15/90)

Acute Inhalation Toxicity

045 91125, "Acute Inhalation Toxicity in Rats - Modification I", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-005, 10/81); 813; S-3206 2.4 lb/G EC, used neat; 0 (air) (5M/5F), and 2.4, 2.9, 3.3, 4.6, 4.7 (10 animals/sex/dose level) mg/l (gravimetric); liquid aerosol inhalation, 1-h, whole body exposure; equivalent aerodynamic diameter (EAD) ranged 3.3 to 4.0 um (GSDs ranged 1.89 to 2.11) w/cascade impactor; Mortality- male: 0/5, 3/10, 2/10, 2/10, 6/10, 9/10, female: 0/5, 4/10, 4/10, 8/10, 9/10, 9/10; Clinical Observations- dyspnea, gasping, tremors, convulsions, hypersalivation, nasal discharge, ocular discharge, decreased body weight gain, prostration, stain on abdomen; Necropsy- included lung congestion, red or dark foci; LC50 (1-h exposure) (M) = 3.72, (F) = 2.75, (M/F) = 3.2 mg/l; Toxicity Category III; **Acceptable. (Duncan, 10/23/90)

Primary Eye Irritation

046 91126, "Eye Irritation Study in Rabbits", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-008, 10/26/81); S-3206 2.4 lb/G EC, dosed neat; 0.1 ml/eye; 6 animals unwashed, 3 animals washed after 30 sec; examined at 24, 48, 72, 96 h, and 7, 10, 13 (unwashed group terminated), 16, 19, 22, 25 d (washed group terminated); UNWASHED- corneal opacity (max. score = 2) with peeling of the epithelium, vascularization, and pannus, which persisted to termination at 13 d; iritis (max. score = 1); and conjunctivitis (max. scores = 3/redn., 3/chem., 3/disch.); WASHED- corneal opacity (max. score = 2) with peeling of the epithelium and vascularization, which cleared by 25 d; iritis (max. score = 1); and conjunctivitis (max. scores = 3/redn., 4/chem., 3/disch.); **Unacceptable** and cannot be upgraded because reversibility was not demonstrated in unwashed eyes. (Duncan,10/16/90)

Although the primary eye irritation study is unacceptable and not upgradeable, there is sufficient information to support a toxicity category I.

Primary Dermal Irritation

047, 006; 91127, 9816, "Primary Dermal Irritation Test in Rabbits", (International Research and Development Corporation, Mattawan, MI, Lab Study No. 491-009, 10/26/81); 815; S-3206 2.4 lb/G EC, applied neat; 0.5 ml/site; two abraded, two intact sites/animal, 6 animals; 24-h exposure, occlusive wrap; examined 24 and 72 h after application and then daily through 14 d (termination); INTACT- erythema of 1-3 and edema of 0-2 at 24 h, erythema of 1 or 2 and edema of 1 at 72 h, erythema of 0-2 and edema of 1 at 96 h, and then erythema and edema of no more than 1 through 14 d; blanching and fissuring were also observed; ABRADED- same range as intact sites; Toxicity Category III; **Acceptable. (Duncan, 10/17/90)

ACUTE STUDIES - Danitol 2.4 EC (formulation CC-17228)

	Toxicity Category
Acute Oral Toxicity LD_{50}	II
Acute Dermal Toxicity LD_{50}	III
Acute Inhalation Toxicity LC_{50}	not submitted
Primary Eye Irritation	I
Primary Dermal Irritation	II

Acute Oral Toxicity

096; 120316; "Acute Oral Toxicity Study in Albino Rats with Danitol 2.4 EC (Formulation CC-17228)" (author: Kiplinger, G.R., WIL Research Laboratories, Inc., Ashland, OH, Lab. Project ID # WIL-194002, 12/11/92); 811; oral; Formulation CC-17228 (30.8% purity); 24 (5M/5F), 51 (5M/5F), 70 (10M/10F), and 200 (10M/10F) mg/kg; Mortality: 0/0, 1/0, 6/10, 7/10, respectively; all clinical signs occurred on day of dosing: clonic convulsion, tremors, salivation, ocular discharge, and abnormal defecation; necropsy revealed reddened renal cortico-medullary junctions, foamy contents in lungs and trachea, dark red lungs and reddened pituitary gland; LD_{50}(M) 84 (51 - 141) mg/kg, (F) = unable to determined, (M/F) = 66 (55 - 80) mg/kg; toxicity category II; **acceptable**; (Leung, 5/5/93).

Acute Dermal Toxicity

096; 120317; "Acute Dermal Toxicity Study in Albino Rabbits with Danitol 2.4 EC (formulation CC-17228)" (author: Kiplinger, G.R., WIL Research Laboratories, Inc., Ashland, OH, Lab. Project ID # WIL 194003, 11/17/92); 812; Danitol 2.4EC (Formulation CC-17228, Lot # CB10L11, 30.8% purity); 2 g/kg applied dermally to intact skin for 24 hours; 1 site/animal; 5 rabbits/sex; no mortalities reported; soft stool were noted for two animals on days 1 or 2; slight to moderate erythema and edema reported at all skin sites and desquamation was present by day 4; two sites had fissuring on days 3 and 4; edema completely subsided by day 12 and slight to moderate erythema were reported at termination (day 14); LD_{50} (M/F) $\geq$ 2 g/kg; toxicity category III; **acceptable**; (Leung, 5/5/93).

Acute Inhalation toxicity

not submitted

Primary Eye Irritation

090; 118073; "Primary Eye Irritation Study in Albino Rabbits with Danitol 2.4 EC (formulation CC-17228)" (WIL Research Laboratories, Inc., Ashland, OH, Lab. Project ID # WIL-194001, 9/11/92); 814; Danitol 2.4 EC (formulation CC-17228, Lot # CB10L11, 30.8% purity); 6 rabbits with unwashed eyes; 0.1 ml; no mortalities were reported; Conjunctivitis (redness 3, chemosis 4, discharge 3) and iritis (grade 1) were noted in treated eye of all animals; corneal opacity (grade 2) occurred in 5 of 6 rabbits and persisted through day 28 for 3 rabbits; iridal irritation cleared by day 21; category I; **acceptable**; (Leung, 10/22/92)

Primary Dermal Irritation

096; 120319; "Primary Dermal Irritation Study in Albino Rabbits with Danitol 2.4 EC (Formulation CC-17228)" (author: Kiplinger, G.R., WIL Research Laboratories, Inc., Ashland, OH, Lab. Project ID # WI. 194004, 9/11/92); 814; Danitol 2.4EC (Formulation CC-17228, Lot # CB10L11, 30.8% purity); 0.5 ml/intact skin site; 6 rabbits; 4 hours; no mortalities were reported; moderate to severe erythema (grade 2-3) and slight edema (grade 1-2) at 72 hours in all animals with desquamation occurring by day 4; edema completely cleared by day 12; slight erythema persisting up to day 20; all signs of skin irritation cleared by day 21; toxicity category II; **acceptable**; (Leung, 5/5/93)

ACUTE STUDIES - Use Dilution of Formulation

044 91124, "The Acute Inhalation Toxicity of DANITOL 2.4 EC (SX-1714) in Rats", (Chevron Environmental Health Center, Richmond, CA, Lab Study No. 2551, 7/15/86); 813; Danitol 2.4 EC, Code No. SX-1714 (32.8% fenpropathrin), diluted to 0.6% v/v in distilled water before use; 0 (air), 5.4 mg/l (gravimetric); 13 ug AI/l (analytical); 39.6 ug Danitol 2.4 EC/l (calculated); 5 animals/sex/-dose level; liquid aerosol inhalation, 4-h, whole body exposure; MMADs (GSD), based on mass of AI, were 3.73 (4.83) and 3.84 (4.35) um, w/cascade impactor; no mortality; Clinical Observations- salivation, nasal discharge, squinted eyes, increased respiration, tremors, ataxia; Necropsy- no abnormalities; Histopathology- no abnormalities; LC50 (M and F) > 39.6 ug Danitol 2.4 EC/l (calculated); **Supplemental.** (Duncan, 11/20/90)

043 91123, "The Acute Inhalation Toxicity of DANITOL 2.4 EC (SX-1714) in Mice", (Chevron Environmental Health Center, Richmond, CA, Lab Study No. 2550, 7/15/86); Danitol 2.4 EC, Code No. SX-1714 (32.8% fenpropathrin), diluted to 0.6% v/v in distilled water before use; [gravimetric (mg/l), a.i. concentration (ug/l), Danitol 2.4 EC concentration (ug/l)]: 0 (air) (5M/5F), 0.48 (5.9, 18.0) (5F), 1.7 (9.8, 30.0) (5M/5F), 4.0 (12.0, 36.3) (5M/5F), 4.9 (13.0, 39.4) (5M/5F); liquid aerosol inhalation, 4-h, whole body exposure; MMADs, based on mass of AI, ranged 1.39-4.34 um (GSDs ranged 2.31-4.92) w/cascade impactor; Mortality- male: 0/5, 0/5, 0/5, 4/5, female: 0/5, 0/5, 1/5, 1/5, 4/5; Clinical Observations- squinted eyes, tremors, elevated gait (hindquarters), hindlimb muscle jerks, phonation, hunched posture, unkempt, anogenital discharge, reduced feces, gasping or labored breathing, collapse, convulsions; Necropsy- no compound-related changes; Histopathology- no-compound-related changes; LC50 (M, calculated) = 37.6 ug/l; LC50 (F,calculated) = 39.1 ug/l (based on Danitol 2.4 EC concentration); **Supplemental Data.** (Duncan, 11/20/90)

041 91121, "Acute Inhalation Toxicity of S-3206 and S-5602 in Mice and Rats", (Institute for Biological Science, Hyogo, Japan, Lab Report No. AT-50-0043, 8/76); 813; S-3206, Lot No. 022018, purity = 97.0%, formulated as a 20% emulsifiable concentrate and diluted in distilled water (0.4-8.0% S-3206) before use; 0 (control not described), 0.0045, 0.0120, 0.0240, 0.0480, 0.0960 mg S-3206/l; 10 mice/sex/dose level and 8 rats/sex/dose level; liquid aerosol inhalation, 3-hour, whole body exposure; particle size not reported; MICE, mortality- male: 0/10, 0/10, 0/10, 0/10, 1/10, 4/10, female: 0/10, 0/10, 0/10, 0/10, 7/10, 8/10; RATS, no mortality; Clinical Observations (same for both species)- salivation, urinary incontinence, lacrimation, tremors, excited state, abnormal respiration, ataxia, decreased body weight gain; Necropsy (same for both species)- no changes attributed to test article; RAT: LC50 (M and F) > 0.096 mg S-3206/l, NOEL (M and F) = 0.012 mg S-3206/l; MOUSE: LC50 (M) = 0.100 (0.0725-0.138), (F) = 0.043 (0.0287-0.0645) mg S-3206/l, NOEL (M and F) = 0.0045 mg S-3206/l; (reported values); **Supplemental.** (Duncan, 11/20/90)

ACUTE STUDIES - Manufacturing Impurities

006 9827, "Acute Oral Toxicity of Two Impurities of S-3206 (Technical) in Mice", (Sumitomo Chemical Company Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-00-0044, 2/81); 811; Para-S-3206 (99.5%) and Benzoin ester of S-3206 (97.2%), tested separately, dosed as solutions in corn oil at a volume of 10 ml dosing solution/kg; 0 (vehicle), 2500, 5000 mg/kg; 10 animals/sex/dose level/test article; no mortality; Clinical Observations (same for both test articles)- decreased spontaneous activity; Necropsy- no remarkable findings; LD50 (same for both test articles) (M and F) > 5000 mg/kg; **Supplemental.** (Duncan, 10/29/90)

006 9826, "Acute Oral Toxicity of 2,2,3,3-Tetramethylcyclopropane Carboxylic Anhydride in Mice", (Sumitomo Chemical Company, Ltd., Pesticides Division, Research Department, Hyogo, Japan, Lab Report No. FT-90-0045, 2/81); 811; 2,2,3,3-tetramethylcyclopropane carboxylic anhydride (purity > 99.0%) (an impurity of S-3206 Technical), dosed as a solution in corn oil at a volume of 10 ml dosing solution/kg; 0 (vehicle) (10M/10F), 500 (10M/10F), 750 (10M), 1000 (10M/10F), 1300 (10M/10F), 1700 (10M/10F), 2200 (10M/10F), 2500 (10M/10F) mg/kg; Mortality- male: 0/10, 0/10, 0/10, 1/10, 2/10, 9/10, 9/10, 10/10, female: 0/10, 0/10, 1/10, 1/10, 4/10, 6/10, 10/10; Clinical Observations-

decreased spontaneous activity, ataxia, limb paralysis, irregular respiration, hyperpnea followed by dyspnea, piloerection, and urinary incontinence at all dose levels; Necropsy- no remarkable changes; LD50 (M) = 1450 (1280-1630), (F) = 1880 (1450-2430) mg/kg; **Supplemental.** (Duncan, 10/29/90)

SUBCHRONIC STUDIES

Oral

055 91135, "Oral Dose Range Finding Study in Dogs", (Hazleton Laboratories America, Inc., Vienna, VA, Lab Project No. 343-123, 10/19/79); 811; S-3206, Lot No. 90403 (purity = 96.2%), dosed in gelatin capsules; 46 (1M/1F), 100 (2M/2F), 464 (2M/2F), 1000 (2M/2F) mg/kg; Mortality- male: 0/1, 0/2, 0/2, 1/2, female: no mortality; Clinical Observations- emesis, salivation, poor pupillary response, tremors, decreased activity, no feces, lack of coordination, mucoid stool, diarrhea, panting; Necropsy- cardiac A-V valve thickened or with a red area, dark spleen, kidney reddened, duodenum hemorrhagic and with a nodule, ileum reddened, dark nodules on cecum, enlarged mesenteric lymph nodes; LD50 (M and F) > 1000 mg/kg (reported); report also contains data for a pair of dogs fed 4000 ppm in diet for four days and then 2000 ppm for eight days; Dogs receiving 4000 ppm in feed exhibited severe emesis and blood mixed with mucoid feces; normal appearance when dogs were returned to control feed; after receiving 2000 ppm for the remaining 8 days, dogs demonstrated no feces and slight tremors; **Supplemental.** (Duncan, 10/12/90)

006, 050; 9810, 91130; "Toxicity Studies on the Insecticide WL-41706: A Three Month Feeding Study in Rats" (Shell Research Limited, London, England, Lab. Report No. FT-71-0001, 5/75); 821; WL-41706 (batch no. 13, 96% purity) in diet containing 2, 10, 50, or 250 ppm to 12 rats/sex/dose; 24 rats/sex were fed control diet; no mortality reported; **no adverse effects indicated;** increased rates of body weight gain occurred, up to week 3 at all dose levels and at 250 and 50 ppm at week 4 in males; this effect was seen only at week 1 in 250, 50, and 10 ppm treated females; minor decreases in adjusted liver weights in 10 ppm males and females; no abnormal changes in clinical chemistry, hematologic indices and pathology reported; NOEL (M/F) $\geq$ 250 ppm (no effects seen at HDT); inadequate dose level selection, target organ not identified; no analysis of diet for actual concentration of test article, and animal husbandry not presented; study **unacceptable** and **not upgradeable;** (Leung, 1/11/91)

006, 051; 9809, 91131; "Toxicity Studies on the Insecticide WL-41706: A Three Month Feeding Study in Rats" (Shell Research Limited, London, England, Lab. Report No. FT-61-0013, 3/76); 821; WL-41706 (Batch No. 24, 97% purity) in diet containing 3, 30, 100, 300, or 600 ppm to 12 rats/sex/dose; 24 rats/sex were fed control diet; no mortality reported; **no adverse effects indicated;** 600 ppm group exhibited pronounced tremors in 9 females and 1 males after 5 weeks which diminished and disappeared by the 11th week; reduced mean body weight in males (5 - 12% of control; p<0.01) and females (8-14% of control, p<0.01) treated at 600 ppm; increases in mean kidney and brain weights for males and females, respectively, and elevated plasma alkaline phosphatase for both sexes at 600 ppm not substantiated by any abnormal pathological changes and were therefore not toxicologically significant; NOEL (M/F) = 300 ppm (based on tremors); study **unacceptable** but **possibly upgradeable** with submission of analysis of diet for actual concentration of WL-41706, rat strain, and animal husbandry; (Leung, 1/10/91).

50489-053,-054,-007; 91133, 91134, 9835; "Subchronic Toxicity Study in Dogs: S-3206"; Dog; 821; Danitol Technical (S-3206); lot# 90403; Hazleton Laboratories America, Inc., Vienna, VA; Project# 343-125; 7/17/80; Dose: Control, 250, 500, 750 ppm (dosed at 1000 ppm through week 3) in the diet; 13 weeks; 6 animals/sex/group; Mortality: 1 male (1000 ppm) sacrificed in extremis-week 3; Observations: treatment-related clinical signs included soft stools, mucoid stools and/or diarrhea, emesis, tremors and ataxia; signs so severe in high dose group that dose level was reduced from 1000 to 750 ppm; severity of signs declined in all dose groups after week 6; Hematology: hematocrit (M/F), hemoglobin (M/F), and rbc count (M/F) were reduced in a dose-dependent manner over the time course of the study; Clinical Chemistry: no treatment-related effects; Urinalysis: no treatment-related effects; Ophthalmology: no treatment-related effects; Body weights, food consumption: weight gain less in the high dose group than controls, food consumption similar for all groups; Necropsy: no treatment-related effects on organ weights, no apparent target organ for the treatment; Histopathology: no treatment-related microscopic alterations; **possible adverse effects indicated:** tremors and ataxia (high dose group); soft stools, diarrhea, and emesis (all dose groups); **NOAEL** can not be determined; Study unacceptable, but may be upgradeable (analyses of the test article in the dietary samples is required in order to confirm the dose levels). (Moore, 1/11/91).

Dermal

** 056; 91136; "21-Day Dermal Toxicity Study in Rabbits" (International Research and Development Corp., Mattawan, MI, Lab. Report No. FT-21-0058, 1/22/82); 822; S-3206 technical (Lot # 1113, 91.4% purity); dermally (0, 500, 1200 or 3000 mg/kg/day) 6 hour exposure/day at 5 days/week for 3 weeks; 5 rabbits/sex/dose; intact and abraded skin; one male rabbit with abraded skin from the 500 mg/kg group found dead on day 18; 3000 mg/kg treated animals exhibited barely perceptible to very slight edema and erythema; no major differences in dermal irritation noted between intact and abraded skin; no compound-related changes in body weight, food consumption, hematology and biochemical parameters were reported; at terminal sacrifice no compound-related macroscopic lesions observed at the application site; microscopic changes observed in treated skin were similar in incidence and severity to those in untreated skin; **no adverse effects**; NOEL(F/M) ≥ 3000 mg/kg (essentially no effects at HDT); study **acceptable**; (Leung, 1/14/91).

057; 91137; "21-Day dermal Toxicity Study in Rabbits" (International Research and Development Corp., Mattawan, NJ, Lab. Report No. FT-21-0059, 1/26/82); 822; S-3206 2.4 lb/G EC (formulated product, Lot No. F1514); dermally (0, 100, 300, or 900 mg/kg) 6 hr exposure/day at 5 days/week for 3 weeks; 5 rabbits/sex/dose; intact and abraded skin; three mortalities occurred during the study: one female in control group, one female at 100 mg/kg and one male at 900 mg/kg; no findings or lesions in tissues examined which would account for the deaths; dermal findings include erythema, edema, fissuring, atonia and desquamation in all treated groups; blanching noted in the 100 and 900 mg/kg groups and coriaceousness in 900 mg/kg group; in all treated groups necropsy indicate test article-related scabbing, crusting, fissuring or thickening of the skin application site; acanthosis, hyperkeratosis, abscess, necrosis, hemorrhage, and ulceration were also reported at application skin site in intact and abraded animals; no compound-related differences in body weight, organ weight, food consumption, hematological and biochemical parameters; **no adverse effects indicated**; NOEL(M/F) < 100 mg/kg (skin irritations); study **unacceptable** but **possibly upgradeable** with submission of analysis of dosing solutions for actual concentration; (Leung, 1/15/91).

METABOLISM STUDIES

Metabolism, Rat

003; 9779; "The Metabolism of WL-41706 in Mammals: The Fate of a Single Oral Dose of [^{14}C]WL-41706 in the Rat" (Shell Research Limited, London, UK, Lab. Report No. FM-51-0002, 8/80); CD rats; 851; [^{14}C-benzyl]WL 41706 (35.8 uCi/mg, radiochemical purity >99.5%); single; oral; 1.5 mg/kg in corn oil; 6 rats/sex; excretion of the test article was rapid in both sexes with 57% and 40% of the dose being eliminated in urine and feces, respectively, 48 hours after treatment; 0.005% of the dose was excreted in expired air; less than 1.5% of the dose remained in the animals 8 days after treatment; low residues found in blood, liver, kidney, fat, muscle and brain 24 hours after dosing were rapidly depleted over the remaining 7 days to barely detectable levels; **supplemental**; (Leung, 11/29/90).

003; 9780; "Metabolic Fate of [^{14}C] WL-41706 in Rats" (Shell Research Limited, London, UK, Lab. Report No. FM-61-0001, 6/76); CD rats; 851; [^{14}C-benzyl]WL 41706 (35.8 uCi/mg), [^{14}C-cyclopropyl]WL 41706 (11.8 uCi/mg) both >99.5% purity; single; oral: 1.5 mg/kg to 6 rats/sex/dose; i.p. dosing of [^{14}C-benzyl]WL 41706 in ethanol (0.1 ml, 18.1 uCi) to 1 female rat; rapid metabolism by cleavage at the ester bond to produce cyclopropanecarboxylic acid and 3-phenoxybenzyl moiety; prior to cleavage, half of the dose undergoes aryl hydroxylation to afford p-hydroxyl-WL 41706, part of which is excreted in the bile as a conjugate and the other portion is cleaved and eliminated in urine as a sulfate of 3-(p-hydroxyphenoxy)benzoic acid and as tetramethyl-cyclopropane carboxylic acid glucuronide; minor portion of the parent compound is hydroxylated at one of the methyl groups of the cyclopropanecarboxylate moiety in the <u>trans</u>-orientation to the carboxyl group; the resultant <u>trans</u>-hydroxyl-WL 41706 is eliminated in the bile as a conjugate, and deconjugated in the feces; part of this metabolite is cleaved to 2-<u>trans</u>-hydroxymethyl-2-methyl-3,3-dimethyl cyclopropanecarboxylic acid which is eliminated in urine; **supplemental**; (Leung, 11/28/90).

007; 9834; "The Effect of Feeding WL-41706 on the Microsomal Mono-oxygenase System of Rat Liver" (Shell Research Limited, London, UK, Lab. Report No. FT-61-0009, 7/76); CD male rats; WL-41706 (batch 266, 97% pure) in diet for 14 days; 0 (diet, 2 rats), and 1, 10, 100, 1000 ppm to 1 rat/dose; dieldrin (100 ppm) to 2 rats used as positive control; positive control functional as demonstrated by increase in mean rate of O-dealkylation of [^{14}C]chlorfenvinphos (0.387 vs 0.024 nmol/min/mg wet liver) and liver weight (17.2 vs 10.8 g) as compared to untreated liver; no evidence for induction of hepatic microsomal enzymes at dietary concentrations up to 1000 ppm for 14 days; results were based on single determination; **supplemental**; (Leung, 11/30/90).

097; 120324; "Excretion, Distribution and Metabolism of [^{14}C] Fenpropathrin Following single or Multiple Dose Administration to Rats (Interim Report - Multiple Dose)" (Authors: Savides, M.C., Ricerca, Inc., Painesville, OH, Lab. Project ID # 91-0238); 851; pretreated with 14 daily oral doses of nonlabeled S-3206 (99% purity) followed by a final dose of [acid-^{14}C]-S-3206 (58.1 mCi/mmole, >99% purity) or [alcohol-^{14}C]-S-3206 (74.9 mCi/mmole, > 99% purity); 0 (corn oil) to 1 rat/sex and 2.5 mg/kg to 10 Sprague-Dawley rats/sex; rats terminated 168 hrs after radiolabeled dose; test article rapidly eliminated in both sexes and essentially complete by 48 hours; 99% of the administered radioactivity found in urine (51.9 - 56.5%) and feces (46.5 - 54.7%) by 7 days after the final dose; greatest concentration of radioactivity was found in fat; about 20% of the administered dose was excreted unchanged in feces; no evidence of bioaccumulation; metabolism of fenpropathrin involves cleavage of the ester bond followed by conjugation with either sulfuric acid or glucuronic acid; oxidation at the methyl group of the acid moiety and hydroxylation at the 4'- position of the alcohol moiety occurs prior to cleavage; **supplemental**; (Leung, 5/3/93)

Although, results from the single low and high dose administrations were not submitted, data from other submitted animal metabolism studies (record numbers: 9779, 9780, and 9834) along with the present study provide adequate information to satisfy the data requirements for an acceptable animal metabolism study.

SB950-MANDATED HEALTH EFFECTS STUDIES

Combined, Rat

** 058; 91138; "S-3206 Potential Tumorigenic and Toxic Effects in Prolonged Dietary Administration to Rats" (Huntingdon Research Centre, Ltd., England, Report No. FT-61-0161, 7/15/86); 835; CD rats; S-3206 technical grade (91.4-92.5% purity) in diet; 0, 50, 150, 450, or 600 ppm to 50 rats/sex/dose; satellite groups: 15 rats/sex/dose; 600 ppm female group was terminated after 52 weeks due to increased mortality rate among males and females receiving 600 ppm and females receiving 450 ppm during first 26 weeks; **possible adverse effect:** body tremors observed among females receiving 600 ppm and to a lesser extent in males receiving 600 ppm and females receiving 450 ppm between weeks 2 and 52; no tumorigenic effects arising from treatment with S-3206; no compound-related effects on food consumption, body weight changes, hematology, clinical chemistry, necropsy and histopathology; NOEL (F) = 150 ppm, (M) = 450 ppm based on body tremors and mortality rate; **acceptable**; (Leung, 12/7/90).

Chronic Toxicity, Rat

006, 010; 9806, 9807, 9854; "Toxicity Studies on the Insecticide WL-41706: Results of physical appearance, survival, body weight, food intake, organ weights, clinical chemistry, hematology and gross pathological observations of rats exposed to WL-41706 for up to two years" (Shell Research Limited, London, UK, Lab. Report No. FT-91-0026, FT-11-0046, FT-10-0048, 12/17/79); 831; COBS rats; WL-41706 (97% purity); 0, 1, 5, 25, 125, 500 ppm in diet for 104 weeks; 24 rats/sex/dose for a.i.; 48 rats/sex for controls; **no adverse effects indicated**; no treatment-related effects were reported in body weights, food intake, survival, clinical chemistry, and hematology; no significant chronic toxic effects attributed to long term feeding of WL-41706 were detected on the basis of macroscopic observation and histopathological examination; increases in spleen (6 months), heart (6 months), and liver (2 years) weights in 125 and 500 ppm female groups; NOEL (M/F) $\geq$ 500 ppm; insufficient dose level and appendices cited in text (record # 9807) were missing; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/29/85; updated Leung, 12/3/90)

052 91132; "Stability of S-3206 in the Diet" (Sumitomo Chemical Co., Ltd., Laboratory of Biochemistry & Toxicology, Hyogo, Japan, Lab. Report No. FP-00-0008, 11/80); S-3206, suspended in corn oil, was mixed with standard feed (final concentration: 300 and 600 ppm) and stored in polyethylene bag at room

temperature (20-28°) for two weeks; stability analysis showed that S-3206 in diet was stable (96.8 - 99.8% of original amount) for two weeks at room temperature; **Supplemental**; (Leung, 11/16/90).

<u>Chronic Toxicity, Dog</u>

** 010, 014, 059; 9851, 33916, 91139; "Chronic Toxicity Study in Dogs S-3206 T.G." (Hazleton Laboratories America, Inc., Vienna, VA, Lab. Report No. FT-41-0122, 11/12/84); beagle dogs; 831; S-3206 (technical grade, Lot # 20514, 92.5% purity) in diet; 0, 100, 250, or 750 ppm to 4 dogs/sex/dose; slightly lower mean body weights for high-dose dogs throughout study; no treatment-related changes reported in food consumption, hematology, clinical chemistry, urinalysis, ophthalmology, gross pathology, and histopathology; clinical signs: one high-dose male found dead during week 32 of study had exhibited ataxia and tremors prior to death; **possible adverse effects**: tremors observed consistently for high-dose dogs and sporadically for mid-dose dogs throughout study; ataxia and languidity noted for high-dose dogs throughout study; NOEL (M/F) = 100 ppm based on tremors, ataxia and languidity; study was originally reviewed and found to be unacceptable but possibly upgradeable with submission of missing appendices (de Vlaming and Gee, 10/30/85); this study was rereviewed with the cited appendices and was found to be **acceptable** (upgraded, Leung, 12/5/90)

<u>Oncogenicity, Rat</u>

see under Combined, Rat above.

<u>Oncogenicity, Mouse</u>

** 060; 91140; "S-3206 Two-Year Feeding Study in Mice" (Huntingdon Research Centre, Ltd., England, Lab. Report No. FT-51-0135, 12/3/85); 832; CD-1 mice; S-3206 technical grade (91.4-92.5% purity) in diet; 0, 40, 150, or 600 ppm to 52 mice/sex/dose; satellite groups: 40 mice/sex/dose; **no adverse effect**; no treatment-related effects on mortality, body weight gain, organ weights, food consumption, efficiency of food utilization, hematological indices, urinalysis, biochemistry and neoplastic lesions; NOEL (M/F) $\geq$ 600 ppm (no effect at HDT) **acceptable**; (Leung, (12/12/90).

061; 91141; "S-3206 Two-Year Feeding Study in Mice: (Terminated after 13 Weeks of Treatment)" (Huntingdon Research Centre, Ltd., England, Lab. Report No. FT-21-0073, 11/82); 832; CD-1 mice; S-3206 (technical grade, 91.4% purity) in diet; 0, 40, 200, or 1000 ppm to 52 mice/sex/dose; satellite groups: 40 mice/sex/dose; study was terminated after 13 weeks of treatment due to high mortality reported among mice receiving 200 or 1000 ppm during the early part of study; **possible adverse effect indicated**: occasional body tremor noted for a few males receiving 1000 ppm from week 1 onwards and for 1 male receiving 200 ppm in week 2; increased (15 - 16 g, $p<0.05$) body weight gain for males receiving 200 or 1000 ppm; slightly higher liver weights for males and females treated at 1000 ppm; no treatment-related effect on food utilization and morphological changes at histological exam were detected; NOEL (M) = 40 ppm (increased mortality and body tremor), (F) = 200 ppm (increased mortality); **supplemental**; (Leung, 12/10/90).

Reproduction, Rat

010, 066, 067, 068; 9852, 9853, 91146, 91147, 91148; "Toxicity Studies on the Insecticide WL-41706: Three Generation Reproduction Study (minus histopathology) in Rats"; (Histopathology data in 068) (Shell Research Ltd., UK (Histopathology - Inveresk Research International, UK, FT-91-0027, 12/17/79); COBS rats; 834; WL-41706 (batch no. 26C, 97% purity); 0, 5, 25, or 250 ppm in diet to 30 rats/sex/group per parental generation - 3 generation study; **no adverse effects indicated**; no compound-related changes in parental body weight, food consumption, and reproductive indices; small reduction in litter size in 250 ppm F-1a litter ($p<0.05$, 89.8% of control) but absent in subsequent top dose litters and therefore not toxicologically relevant; changes in pup weight were inconsistent with respect to time and magnitude; pathological examination revealed hydrocephalus in 250 ppm pups from F-1b litters (1/329, $p=0.475$) and 5 ppm and 250 ppm pups from F-3b litters (1/135, $p=0.369$ and 1/212, $p=0.479$; respectively); maternal NOEL = developmental NOEL $\geq$ 250 ppm; insufficient dose level selection; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 11/4/85; updated Leung, 1/7/91).

** 069; 91149, 91150; "Effect of S-3206 on Multiple Generations of the Rat" (Huntingdon Research Centre, Huntingdon, England, Lab. Report No. FT-61-0159, 7/4/86); COBS rat; 834; S-3206 (batch no. 20514, 92.5% purity); 0, 40, 120, or 360 ppm in diet to 17-28 rats/sex/group per parental generation - 3 generation study; no effect on mating performance of surviving animals; no mortality among males; **possible adverse effect**: dose-related mortality in F-1b generation females during lactation at mid and high dose; second and third week post partum females exhibited body tremors with associated spasmodic muscle twitches and increased sensitivity at high and mid dose levels; three F2b pups at mid dose showed body tremors prior to weaning, two of which subsequently died; histopathological examination did not reveal any abnormalities associated with treatment; maternal NOEL = 40 ppm (based on tremors and unscheduled deaths), paternal NOEL $\geq$ 360 (no effect at HDT); systemic NOEL = 40 ppm (based on F2b pups at mid dose showing tremors); reproductive NOEL = 120 ppm (based on decreased litter size and pup weight); study **acceptable**; (Leung, 1/9/91)

Teratology, Rat

008, 062; 9840, 91142; "Teratology Study in Rats, Final Report" (Hazleton Laboratories America, Inc., Vienna, VA, Lab. Report # FT-01-0031 with addendum, 9/87); Fischer 344 Rats; 833; S-3206 (lot# 90403, 96.2% purity); oral intubation; 0, 0.4, 2.0, 10 mg/kg/day in corn oil to 27-28 females/dose on days 6-15 of gestation; **possible adverse effects indicated**: tremors observed in some high dosed females following first dose and one subsequent day during the treatment period; mortality in one mid-dose and nine high-dose females (including 2 of which were not pregnant); decrease in body weight gain (73% of control, $p<0.05$) due to reduced food consumption (85% of control, $p<0.05$) at HDT during treatment period; increased incidence of clinical signs (blood crust on eye, lacrimation, and red eye) reported for HDT; fetal death observed in the litter of one control and one mid-dose female; one dead fetus (control) appeared edematous and another dead fetus (mid dose) was edematous and exhibited hydrocephaly and gastroschisis; maternal NOEL = 0.4 mg/kg/day (based on tremors and unscheduled death); developmental NOEL $\geq$ 10.0 mg/kg/day (no effect at HDT); study was originally unacceptable but possibly upgradeable of missing appendices and individual data (de Vlaming and Gee, 11/4/85); study **unacceptable** but **possibly upgradeable** with submission of dose analysis; (Leung, 12/26/90).

** 063; 91143; "Rat Teratology Study with S-3206" (Hazleton Laboratories America, Inc., Vienna, VA, HLA Study No. 343-216, 3/13/90); S-3206 (Lot # 70711, 91.9% purity); oral; 0 (corn oil), 0.4, 1.5, 2, 3, 6, or 10 mg a.i. /kg/day in corn oil to 30 female CDF•(F-344)/CrlBR rats on days 6 to 15 of gestation; **possible adverse effect:** unscheduled deaths in 7 pregnant rats, tremors, ataxia, and convulsions in rats treated at 10 mg/kg/day; decrease in maternal body weight gain (87 % and 70% of control, $P \leq 0.05$) at 6 and 10 mg/kg/day, respectively; microphthalmia noted in one fetus in each dose group (0, .4, 1.5 and 10 mg/kg/day) but was not dose-related; incomplete ossification of the 5th/6th sternebra reported in all dose groups; no evidence of embryotoxicity, fetal toxicity, or teratogenicity was reported at any dose level; maternal NOEL = 3 mg/kg/day (based on tremors, ataxia, convulsions, decreased body weight gain, and unscheduled deaths); developmental NOEL ≥ 10 mg/kg/day (no effects reported at any dose level); study **acceptable** (Leung, 12/28/90).

Teratology, Rabbit

008, 064; 9839, 91144; "Toxicity of WL-41706: Teratological Studies in Rabbits Given WL-41706 Orally" (Shell Research Limited, London, England, Lab. Report No. FT-51-0006, 8/80); Dutch rabbits; 833; WL-41706 (batch 24, 97% purity); oral by gelatin capsule; 0, 0 (corn oil), 1.5, 3.0, 6.0 mg/kg/day to 20-31 females/dose on days 6-18 of gestation; **no adverse effects indicated;** maternal NOEL = developmental NOEL > 6 mg/kg/day (no effects observed with highest dose tested); no justification of dose levels employed; no in-life observation, food consumption data, animal husbandry, and individual data reported; study **unacceptable but possibly upgradeable** with submission of additional data to correct deficiencies as indicated above; (de Vlaming and Gee, 11/4/85; updated Leung, 12/27/90).

** 065; 91145; "The Effect of S-3206 on Pregnancy of the New Zealand White Rabbit" (Huntingdon Research Centre, Ltd., Huntingdon, England, Lab. Report No. FT-51-0134, 11/13/85); 833; S-3206 (batch no. 20514, 92.5% purity); oral gavage; 0 (corn oil), 4, 12, or 36 mg/kg/day to 17-19 females/dose on days 7-19 of gestation; **possible adverse effect:** unscheduled death in 1 pregnant rabbit at high dose; 2 rabbits (including 1 of which is non-pregnant) exhibited shaky movements/trembling at high dose; dose-related increase in the incidence of grooming after dosing; no gross macroscopic changes attributed to treatment were reported; one dam upon autopsy had an interrupted right uterine horn; no treatment-related effects on litter parameters or the incidence of malformations, anomalies, or skeletal variations; maternal NOEL = 12 mg/kg/day (based on shaky movements/trembling); developmental NOEL ≥ 36 mg/kg/day (no effect at HDT); study **acceptable;** (Leung, 1/2/91).

Gene Mutation

** 009, 071; 9842, 91152; "Gene Mutation Test of S-3206 in Bacterial System" (Takarazuka Research Center, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0107, 3/19/84; addendum: FT-40-0115, 3/12/84); S-3206 technical (Lot # 20514, 92.5% purity); tested with *Salmonella typhimurium* strains TA-98, TA-100, TA-1535, TA-1537, TA-1538, *Escherichia coli* strain WP2uvrA (trp-) with and without activation by PCB (Kanechlor-400)-induced rat liver S9 fraction; duplicate plates; two trials; concentrations of 0(DMSO), 50, 100, 500, 1000, and 5000 ug/plate; 20 minute preincubation period or exposure to S-3206 before plating; 48 hr incubation; positive controls functional; **no adverse effects indicated:** no increase in revertants reported; after initial review, study was found to be **unacceptable** but **possibly upgradeable** with submission of individual data; (de Vlaming and Gee, 10/29/85); study rereviewed with individual plate values subsequently submitted as an addendum; **acceptable**; (Leung, 12/13/90).

009; 9847; "Studies on Mutagenicity of Some Pyrethroids on Salmonella Strains in the Presence of Mouse Hepatic S9 Fractions" (Institute for Biological Science, Hyogo, Japan, Lab. Report No. AT-70-0157, 8/4/77); S-3206 (Lot No. 22018, 97% purity); tested with Salmonella typhimurium strains TA-98, TA-100, TA-1535, TA-1537, TA-1538 with activation by PCB-induced mouse (6 strains) S9 fraction; 3 replicates; 1 trial; (DMSO), 10, 100, or 1000 ug/plate; 48 hr incubation; positive controls were not functional with TA-1537 strain; **no adverse effects indicated:** no increase in revertant colonies reported; individual data not reported; no justification for dose levels and the use of mice rather than rat hepatic S9 fractions; cell survival not measured; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/28/85; updated Leung, 12/14/90).

009, 070; 9849, 91151; "An Assessment of the Mutagenic Potential of S-3206 Using an In Vitro Mammalian Cell Test System" (Huntingdon Research Centre, England, Lab. Report No. FT-21-0060, 3/25/82); S-3206 technical (batch No. 01113, 91.4% purity); tested with L5178Y TK +/- cells (3.7.2C) with and without activation by aroclor 1254-induced rat liver S9 fraction; 2 replicates/dose; 1 trial; 3 hour incubation; concentrations of 0 (DMSO), 50.3, 84.5, 141.9, 238.2 without S9 activation, concentrations of 0 (DMSO), 47.5, 75.3, 119.4, 189.2 with S9 activation; positive control functional; **no adverse effects indicated:** no increase in mutation frequency/10^6 survivors seen without S9 activation; result with S9 activation equivocal; no repeating or confirming trial; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 20/28/85; updated Leung, 12/17/90).

Chromosome Effects

** 009, 073; 9841, 91154; "In Vitro Sister Chromatid Exchanges Test of S-3206 in CHO-K1 Cells with Addendum, Comments and EPA Review" (Biochemistry & Toxicology Laboratory, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0108, 3/19/84); S-3206 technical (Lot # 20514, 92.5% purity); tested in Chinese hamster ovary cells (CHO-K1) with and without activation by PCB-induced rat liver S9 fraction; concentrations 0 (DMSO) and a dose range of 3 x 10^{-6} to 10^{-4} M; 4 cultures/dose; 2 trials; 2 hr exposure followed by 28 hr incubation period with Brdu; 50 cells/dose scored for sister chromatid exchange; positive controls functional; **no adverse effects indicated:** S-3206 does not induce any SCE in CHO-K1 cells in the presence or absence of S9 activation; study **acceptable**; (Leung, 12/20/90).

009; 9843; "Micronucleus Test of S-3206" (Takarazuka Research Center, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report No. FT-40-0106, 3/19/84); S-3206 technical (Lot # 20514, 92.5% purity); single i.p.; 0 (corn oil), 50, 100, or 200 mg/kg; high dose group repeated in second experiment; mitomycin C (2 mg/kg, positive control); 6 male ICR mice/dose group; bone marrow samples taken at 24 hrs plus 48 and 72 hrs for 200 mg/kg after dosing; positive control functional; **no adverse effects indicated:** S-3206 does not induce micronuclei in bone marrow erythrocytes of mice; individual data not reported; no justification for using only male animals; study **unacceptable** and **not upgradeable**;(de Vlaming and Gee, 10/29/85; updated Leung, 12/18/90).

009; 9848; "Toxicity Studies with WL-41706: Chromosome Studies on Bone Marrow Cells of Chinese Hamsters After Two Daily Oral Doses of WL-41706" (Shell Research Limited, London, England, Lab. Report No. FT-51-0003, 12/75); WL-41706 (batch # 24, 97% purity); tested in Chinese hamsters; two successive daily oral doses: 0 (DMSO), 10 or 20 mg/kg; cyclophosphamide (100 mg/kg, positive control); 5-6 hamsters/sex/dose; 2 trials; 90 minutes before termination at 8 and 24 hrs after second dose, rats were treated with 0.01 ml of 0.04% Colcemid solution/g body weight (i.p.); 100 cells analyzed from the bone marrow of each animal; positive control functional; **no adverse effects indicated:** two daily oral doses of WL-41706 did not induce any demonstrable chromosome damage in Chinese hamster bone marrow cells at either sampling time interval; individual data not presented, mitotic index not reported, no justification of dose level, and criteria for scoring not included; study **unacceptable** and **not upgradeable**; (de Vlaming and Gee, 10/28/85; updated Leung, 12/18/90).

** 072; 91153; "In Vitro Chromosomal Aberration Test of S-3206 in Chinese Hamster Ovary Cells (CHO-K1)" (Biochemistry & Toxicology Laboratory, Sumitomo Chemical Co., Ltd., Hyogo, Japan, Lab. Report# FT-90-0200, 5/17/89); S-3206 technical (Lot # 20514, 92.4% purity); tested in Chinese Hamster Ovary Cells with and without activation by PCB-induced rat liver S9 fraction; 100 cells from each duplicate/dose scored for chromosomal aberrations; single trial; concentrations 0 (DMSO) and a dose range of 10 - 1000 ug/ml; 2 and 18 to 24 hr exposure with and without S9 activation, respectively; positive control functional; **no adverse effects indicated:** S-3206 did not induce any significant increases in the frequencies of cells with structural aberrations both in the presence or absence metabolic activation; study **acceptable;** (Leung, 12/19/90)

DNA Damage

009; 9846; "Toxicity Studies with WL-41706: Mutagenicity Studies with WL-41706 in the Host-Mediated Assay"(Shell Research Limited, London, England, Lab. Report No. FT-61-0007, 8/80); WL-41706 (batch No. 24, 97% purity); mitotic gene conversion in Saccharomyces cerevisiae strain JD1 after oral dosing of CF male mice with WL-41706 at 0 (DMSO), 10, or 20 mg/kg; ethyl methanesulfonate (EMS, 400 mg/kg); 4 replicates/dose; 3 trials; positive control functional; **no adverse effects indicated:** no increase mitotic gene conversion detected; study **unacceptable** but **possibly upgradeable** with submission of individual data, dose level and animal specie justification, and evidence that the test article is absorbed and reaches peritoneal cavity after oral administration; (de Vlaming and Gee, 10/28/85; updated Leung, 12/13/90).

** 009; 9844; "Autoradiographic Assessment of DNA Repair in Mammalian Cells After Exposure To S-3206 (Fenpropathrin)"(Huntingdon Research Centre, Cambridgeshire, England, Lab. Report No. FT-21-0068, 6/16/82); S-3206 technical (Lot # 1113, 91.4% purity); tested with HeLa S3 cells with and without activation by aroclor 1254-induced rat liver S9 fraction; concentrations 0 (DMSO) and a dose range of 200 - 3200 ug/ml; precipitation occurred at $\geq$ 100 ug/ml; 2 replicates; 3 trials; 90 or 180 minute exposure; positive controls in the presence of S9 activation were borderline in increase in number of silver grain; **no adverse effects indicated:** treatment with S-3206 did not result in any significant increase in unscheduled DNA synthesis by autoradiography; study **acceptable** (de Vlaming and Gee, 10/28/85; updated Leung, 12/21/90)

009; 9850; "Studies on DNA-damaging Capacity of S-3206 with Bacillus subtilis" (Research Dept., Sumitomo Chemical Co., Ltd., Osaka, Japan, Lab. Report No. FT-00-0038, 8/80); S-3206 technical (Lot # 22018, 97% purity); tested with Bacillus subtilis M45 rec^- and H17 wild type strains without activation; 4 plates/dose; 2 replicated trials; 24 hr incubation; dose range of 0 - 5000 ug/paper disk; positive control functional; **no adverse effects indicated:** S-3206 did not exhibit any inhibition of growth with either strain; no test or evidence of diffusion of test article in agar; no justification for dose level selection; individual data not reported and growth inhibition of both strains in the presence of metabolic activation not investigated; study **unacceptable** and **not upgradeable;** (de Vlaming and Gee, 10/28/85; updated Leung, 12/20/90).

Neurotoxicity

50489-007; 09836; Acute Delayed Neurotoxicity; 817; Rat; Shell Research Limited, Sittingbourne Research Sittingbourne, Kent, England, Report # TLGR.0041.76, June 1976; WL 41706; 6/sex/dose; 1 dose of 900 ppm in diet (exposure duration not explicitly stated); mortalities- males: 2/6; females: 6/6; observations- males: fine tremors on day 2 after initial exposure, with tremors becoming violent along with erratic jumping behavior in 3/6 by day 12 with one found dead on day 16, another found dead on day 20, with tremors persisting in 4/6 at day 25; females: tremors in all after exposure, with all dead or sacrificed due to morbidity by day 5; necropsy- swelling and disintegration of nerve axons in all with the exception of 1/6 males; **possible adverse effect indicated:** swelling and disintegration of nerve axons; **Reported NOEL=NOAEL< 900 ppm.** Very brief report. Full report needed to determine acceptability of study. (Corlett, 11/15/90)

50489-049; 91129; Acute Delayed Neurotoxicity; 817; Hen; Shell Research Limited, Shell Toxicology Laboratory, Tunstall, England, Report TLGR.0068.77, August 1977; WL 41706; 6 hens/group; 5 successive (unprotected) daily doses of 1 g/kg (dosing regime repeated 3 weeks later); positive control (0.5 ml/kg TOTP); negative control (no treatment); no mortalities; observations- positive control: signs of neurological disturbance beginning by the 16th day becoming progressively worse over the following 9 days with histological examination showing degenerating myelin and swollen axons in the sciatic nerve and degenerating myelin in the spinal cord; experimental and negative control groups: no signs of neurological disturbance and no histological lesions found; NOEL = NOAEL $\geq$ 1 g/kg; **Supplemental** (a dose of 1 g/kg was used, although the oral LD_{50} was greater than 1.5 g/kg). (Corlett, 11/14/90)

CONCLUSIONS: Do data support registration?

Toxicity data for Danitol 2.4 EC and the active ingredient, fenpropathrin, were submitted to support a Section 3 registration request.

The primary dermal irritation study using S-3206 technical is unacceptable but possibly upgradeable with submission of additional data verifying that the material is a liquid prior to skin site application. However, data from an acute dermal toxicity study conducted in rabbits supports a toxicity category IV. Although the primary eye irritation study conducted with the formulated product (S-3206 2.4 lb/G EC) is unacceptable and not upgradeable because the observation period was inadequate for ascertaining the reversibility of corneal damage, there is sufficient information to support a toxicity category I. An acute inhalation toxicity study with the technical active ingredient was not submitted and is not required at this time because the test article has a low melting temperature and can not be milled to produce an inhalable aerosol. All other acute oral, dermal, and inhalation toxicity and primary skin and eye irritation studies on S-3206 technical and formulated product (Danitol 2.4 EC) are acceptable.

Individual metabolism studies when considered collectively satisfy the current data requirements necessary for a complete metabolism study.

One of the three subchronic oral toxicity studies in rats is unacceptable because the dose levels selected did not elicit any signs of toxicity and were inadequate to permit identification of target organs. The other subchronic oral toxicity studies in rats and dogs are unacceptable but may be upgraded with submission of analysis of test article in the diet to confirm dose levels.

The 21-day dermal toxicity studies in rabbits conducted with S-3206 technical is acceptable. In contrast, the other 21-day dermal toxicity study conducted with Danitol 2.4 EC product is unacceptable but may be upgraded with analysis of the dosing material for content. This study also indicates that Danitol 2.4 EC produces severe skin irritations after exposure.

The combined chronic/oncogenicity study in rats is acceptable. The chronic toxicity study in dogs is acceptable. The oncogenicity study in mice is acceptable. The increased incidence of pulmonary adenoma and/or adenocarcinoma in males and females from the low-dose and males from the mid-dose groups from the latter study is not interpreted as a possible adverse effect because the overall incidence of pulmonary tumors did not demonstrate any dose-response relationship.

One of the two reproductive toxicity studies in rats is not acceptable and not upgradeable because the dosage levels selected did not elicit any signs of toxicity in order to provide a meaningful evaluation. The other reproductive toxicity study in rats is acceptable.

Acceptable teratology studies conducted in rats and rabbits have been submitted. However, there are teratology studies conducted in rats and rabbits which are unacceptable but possibly upgradeable with submission of additional data as indicated in the one-liner.

Acceptable studies were submitted to fulfull the data requirements for the gene mutation, structural chromosomal aberration, and other genotoxic effects categories.

An acute delayed neurotoxicity study in rat was submitted. The study report was too brief to determine its acceptability and a full report would be needed for evaluation. Swelling and disintegration of nerve axons were reported and are interpreted as a possible adverse effect. Data from other studies submitted for evaluation provide adequate information in characterizing the neurotoxicity associated with exposure to the active ingredient or to Danitol 2.4 EC.

Tremors, ataxia and sometimes convulsions have been observed in the test animals following acute exposure as indicated by the oral and dermal toxicity studies using the technical active ingredient or Danitol 2.4 EC, where the NOEL ranged from 10 - 100 mg/kg. Acute exposure to the formulated product (S-3206 2.4 lb/G EC) by the inhalation route also produced tremors and convulsions in all dose groups with 2.4 mg/l as the lowest dose tested. In addition, chronic exposure to the technical grade active ingredient has been shown to produce tremors as demonstrated in the combined chronic/oncogenicity study in rats (NOEL: female - 150 ppm, male - 450 ppm) and chronic feeding study in dogs (NOEL = 100 ppm). Furthermore, second and third week post partum female rats in a reproductive toxicity study exhibited body tremors with associated spasmodic muscle twitches at the mid- and high-dose levels (120 and 360 ppm, respectively; NOEL = 40 ppm). Three F2b pups at the mid-dose level also showed body tremors prior to weaning (Developmental NOEL = 40 ppm). Similar observations were also reported in teratology studies where the maternal NOEL for rats and rabbits are 3 and 12 mg/kg/day, respectively. The observations of tremors, ataxia, and convulsions have been associated with mortalities as demonstrated in the rat teratology study and are therefore interpreted as an adverse effect.

RECOMMENDATIONS: What type of registration action is being considered? In the case of ongoing registration, register or do not register? What other specific studies or data are requested?

Submitted as as new active ingredient Section 3 registration request.

The data are adequate to make a complete toxicological evaluation of the subject product.

Product label identifies all potential hazards indicated by the data reviewed.

Decision regarding registration will be deferred until the SB950 Adverse Effects Advisory Panel completes its risk assessment prioritization.

Peter Leung — 5/6/93
Peter Leung, Ph.D. — Date
Staff Toxicologist

G. T. Patterson — 5/7/93
Gary Patterson, Ph.D. — Date
Senior Toxicologist

C. Gee — 5/7/93
Joyce Gee, Ph.D. — Date
Senior Toxicologist

APPENDIX B

Acute Dietary Exposure

FENPROPATHRIN (Danitol®)

DIETARY EXPOSURE AND ACUTE TOLERANCE ASSESSMENTS

Wesley C. Carr, Jr.

HEALTH ASSESSMENT SECTION

MEDICAL TOXICOLOGY BRANCH

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

May 17, 1994

Fenpropathrin Dietary Summary

Acute and chronic dietary exposures and an acute tolerance assessment were performed for the pesticide fenpropathrin using a NOEL of 3.0 mg/kg/day for the acute analyses. Two primary and twenty secondary raw agricultural commodities (RAC) were assessed. The residue data were either registrant supplied field trial data or U.S. EPA tolerances. The majority of the residue values were derived from the registrant supplied information. The cotton residue values were: acute; 0.29 ppm, and for chronic; 0.069 ppm. The tomato residue values were: acute; 0.07 ppm and for chronic; 0.055 ppm. Dietary concentration adjustment factors were used since fenpropathrin residues were found to concentrate in refined cotton oil and soapstock and tomato canning waste. There were three scenarios evaluated for impact on the secondary residues; cotton source residues, tomato source only, and cotton and tomato origin of residues that could be found on animal feed. The non-beef red meat residues were surrogates derived from a beef study using fenpropathrin administered in the diet. The red meat and milk residues varied depending on the RAC combinations. The milk residue ranges were: acute; 0.01-0.03 ppm, for chronic; 0.005-0.019 ppm. Beef tissues residues ranged from 0.01-0.02 ppm for acute, to 0.006-0.019 ppm for chronic. Poultry meat and egg residues from the chicken dietary feeding study varied depending on the potential residue contribution from cotton and tomato sources. The poultry and turkey meat residue values were surrogates derived from the registrant chicken dietary feeding study. The chicken egg residues for acute were 0.01 ppm and 0.005 for chronic. The poultry meat tissues ranged from 0.01-0.02 ppm for acute, to 0.01 ppm for chronic. The margins of safety were equal to or greater than 2,296 (Children 1-6 years) for acute exposures from all three possible dietary contribution scenarios. An acute tolerance assessment was performed on the 10 main individual temporary tolerances. The margins of safety were greater than 875 for each of the individual commodities. The lowest acute tolerance margin of safety was 876 for Non Nursing Infants (<1 year) consuming milk.

Fenpropathrin Pesticide Dietary Residue Information

Fenpropathrin (40 CFR #180.466) acute tolerance, acute, and chronic non-oncogenic dietary exposure assessments were initiated and completed in 1994 (18, 19). No chronic oncogenic dietary was performed as no oncogenic endpoint was identified in the Department of Pesticide Regulation (DPR) toxicology database or risk assessment. All available fenpropathrin raw agricultural commodity (RAC) residue data (17) and residues from potential secondary sources were evaluated (see Table 1). The U.S. EPA fenpropathrin 40 CFR 180.466 tolerance is characterized as fenpropathrin parent material alone with no significant fenpropathrin metabolites listed in the tolerance (4). Therefore, at the present time, only fenpropathrin parent material will be routinely monitored for by federal and state regulatory agencies.

The Valent Company's primary compound identified in the submitted field residue and feeding studies was fenpropathrin, CAS# 39515-41-8, [(RS)-α-cyano-3-phenoxybenzyl-2,2,3,3-tetramethylcyclopropanecarboxylate] (17). The two main metabolites are TMPA, CAS# 15641-58-4, (1,1,2,2-tetramethylcyclopropane carboxylic acid) and PBA, CAS# 3739-38-6, (3-phenoxybenzoic acid). The residue concentration and dietary fate of fenpropathrin and its TMPA and PBA metabolites were all evaluated by Valent, Inc. and the results were reported in the various submitted registrant studies (11, 12, 13, 16). The registrant analytical method for residue characterization of fenpropathrin parent material has a minimum detection level (MDL) of 0.01 ppm (5, 15). TMPA and PBA metabolites are characterized by the same residue analytical method and the MDLs for each is 0.02 ppm (5, 11, 12, 13, 15, 16).

The FDA limit of quantitation (LOQ) level for fenpropathrin is 0.02 ppm (9). The FDA fenpropathrin detection method is part of their multiple residue screen however, it is not part of the routine Luke extract method. The FDA fenpropathrin method requires a florisil cleanup of the routine Luke method. The expense and time required for the cleanup method reduced the number of potential samples the could be analyzed for fenpropathrin residues in the FDA program from about 20,000 per year to approximately 3,000 in 1992 and around 2,700 in 1993 (1990 total unavailable). The FDA has looked for, but has not found, any fenpropathrin residues beginning with fiscal year 1991 and continuing on with 1992 and 1993 (9).

The USDA Food Safety Inspection Service (FSIS) meat monitoring program has not monitored for fenpropathrin residues as of the time of issue of the 1992 USDA Blue Book. The USDA FSIS residue analytical capability for fenpropathrin is 1.0 ppm for fat in all farm animal species (20, 21).

The DPR fenpropathrin parent material MDL, using a gas chromatograph/mass spectrophotometer with electron capture detector method (GC-/MS-/ECD), is 0.2 ppm for tomatoes on the multiple residue screen. This is the only RAC/pesticide combination identified by the DPR chemistry laboratory at the present time (1). No fenpropathrin residues have, as yet, been identified by the DPR pesticide monitoring programs (6).

Usage

Cotton and tomatoes, both fresh market and processing, are extensively produced in California (2, 3, 22, 23). The DPR 1991 and 1992 pesticide use report annuals do not show any applications of fenpropathrin on RACs in California (7, 8). There was a U.S. EPA issued 1993-1994 (one year) section 18 for use on California grown tomatoes (10). No fenpropathrin California applications on tomatoes were reported as being made in the 1992 DPR pesticide use report or the USDA National Agricultural Statistical Service (NASS) 1992 vegetable crop summary (8, 23).

The USDA NASS vegetable crops 1992 reported the use of fenpropathrin on about 14% of the major U.S. fresh tomato acreage in 1992. The entire U.S. fenpropathrin usage occurred on Florida grown fresh market tomatoes (23). The eight major fresh market tomato production states are; CA, FL, GA, MI, NJ, NY, NC, and TX. There was no reported fenpropathrin use on processing tomatoes in 1992 (23). The U.S. EPA granted a section 18 petition to Florida for 50,000 acres of tomatoes for the 1993 use season (26).

Special Raw Agricultural Commodity (RAC) Adjustment Factors

Primary RAC Residues (cotton and tomato)

Cotton

The registrant has requested a California section 3 registration for cotton. The U.S. EPA temporary tolerances include cottonseed products; 1.0 ppm section 408 raw food tolerance for cottonseed, 3.0 ppm section 409 processed food additive tolerance for cottonseed oil, and a 2.0 ppm section 409 feed additive tolerance for cottonseed soapstock (26, 27). The registrant has submitted cotton field trials and processed products residue data for DPR evaluation (13).

Table 1. Summary of Fenpropathrin Residues as of May, 1994 (25).

RAC	Source[1] (reference)	Tolerance (ppm)	Residue (ppm) Acute	Chronic	N	Value Selected
Beef, fat	EPA/REG (5, 11, 27)	0.02	0.02	0.012	3	Toler./extrap. residue
Beef; meat, MBYP	Reg-f (5, 11, 27)	0.02	0.01	0.01	3	Extrapolated residues
Cottonseed (meal, oil)	Reg-fp (13, 14)	1.00	0.29	0.069	14	Measured residues
Eggs	Reg-fd (12, 15)	0.02	0.01	0.005	14	Measured residues
Goat, fat[2]	EPA/REG (11)	0.02	0.02	0.012	3	Toler./extrap. residue
Goat; meat, MBYP	Reg-f (11)	0.02	0.01	0.01	3	Extrapolated residues
Horse	Reg-f (11)	0.02	0.01	0.01	3	Extrapolated residues
Milk	Reg-fd (11)	0.03	0.01	0.005	44	Measured/ext. residues
Milk, fat	Reg-fd (11)	0.03	0.03	0.019	44	Toler./extrap. residue
Pork, fat	EPA/REG (11)	0.02	0.02	0.012	3	Toler./extrap. residue
Pork, meat, MBYP	REG-f (11)	0.02	0.01	0.01	3	Extrapolated residues
Poultry, fat	EPA/REG (12, 15)	0.02	0.02	0.012	3	Toler./extrap. residue
Poultry, meat, MBYP	REG-f (11)	0.02	0.01	0.01	3	Extrapolated residues
Sheep, fat	EPA/REG (11)	0.02	0.02	0.012	3	Toler./extrap. residue
Sheep, meat, MBYP	REG-f (11)	0.02	0.01	0.01	3	Extrapolated residues
Tomato	REG-fp (16)	N.A.	0.07	0.055	4	Measured residues

1/ **DPR** = Department of Pesticide Regulation, **EPA** = U.S. Environmental Protection Agency, **Reg-f** = Registrant supplied field residue data, **Reg-fd** = Registrant supplied animal feeding study, **Reg-fp** = Registrant supplied field residue study with post harvest processing data.
2/ **N** (Sample) = All red meat residue values based on surrogate from beef feeding study residue data.

The data volumes contained pre-1989 (1983-1987) and 1989 cotton field trails data. The pre-1989 data were all derived from 0.2 lbs active ingredient (a.i.)/acre rates which are below the currently requested rate of 0.3 lbs a.i./acre. These data from the 25 pre-1989 studies were not used in the DPR dietary analysis. The seven 1989 cotton field trials were conducted using five applications at the fenpropathrin rate, as 2.4 EC, of 0.3 lbs a.i./acre with a 21 day preharvest interval (PHI) which are the maximum label requested rates. The RAC and processing residue data from these trials were used in the DPR analysis.

The 1989 cotton field trials highest measured cottonseed residue value was 0.29 ppm which is the value used for the acute residue. There were two replications for each of the 7 field trials resulting in 14 data points (0.02, 0.02, 0.01, 0.01, 0.29, 0.27, 0.04, 0.07, 0.07, 0.05, 0.03, 0.02, 0.03, and 0.04 ppm) with an arithmetic mean of 0.069 ppm and a sample standard deviation of 0.088 ppm. The mean of 0.069 ppm is used as the DPR chronic residue value.

The cottonseed products processing residue fate were examined in three pre-1989 field studies. Even through the pre-1989 residue values were not used, all three trials processing results indicated that fenpropathrin residues would likely concentrate by 3 fold in the refined oil and by 2 fold in the soapstock. There appeared to be no concentration of residues in hulls or cottonseed meal. The DPR dietary analysis has two available cottonseed food form codes; cottonseed oil and meal (18, 19). The analysis sets the dietary program's adjustment factor #1 to 3.0 (usual for cottonseed oil is 1.0) for the cottonseed-oil food form in both the acute and chronic sections. This will account for potential residues that may concentrate in this product and potentially end up in the feed of domestic farm animals (24).

Tomato

The registrant has a current California section 18 registration for tomatoes granted by the U.S. EPA (10). The current, available U.S. EPA temporary tolerances list does not include a tomato temporary tolerance. The tomato residue value selected by DPR is based on registrant supplied field trial data. The registrant has submitted tomato field trial and processed products residue data for DPR evaluation (16). The data volumes contained the results from eight 1989 and 1990 tomato field trails conducted in Florida. The two years of data considered by DPR were all derived from the 0.2 lbs a.i./acre rates with a five day PHI which was the closest to the currently existing California section 18 rate and 7 day PHI. Data from six of the studies were not used in the DPR dietary analysis. These residue data were not used because the studies did not include treatments of 5 day PHI (the longest PHI tested), fenpropathrin alone applications within their trials. The two 1989 tomato field studies evaluated and selected had the fenpropathrin alone and five day PHI treatment in addition, one of the trials had a processing of cottonseed residues component. The two studies were conducted using six applications at the fenpropathrin rate, as 2.4 EC, of 0.2 lbs a.i./acre with a 5 day preharvest interval which are the closest available to the California seven day PHI, 0.2 lbs a.i./acre requested rate. The RAC and processing residue data from these trials were used in the DPR analysis.

The 1989 tomato field trials highest measured mature green fruit residue value was 0.07 ppm which is the value used for the acute residue value. There were two replications for each of the 2 field trials resulting in 4 data points (0.06, 0.04, 0.05, and 0.07 ppm) with an arithmetic mean of 0.055 ppm and a sample standard deviation of 0.011 ppm. The mean of 0.055 ppm is used as the DPR chronic residue value unless otherwise characterized.

The tomato components processing residue fate was examined in one 1989 field study. The 1989 processing residue values were not used because the PHI interval was only three days. However, the magnitude of concentration factors and effects of processing were considered in the DPR selected residues. The processing results, from the 1989 field study #T-7464, indicated that fenpropathrin residues would likely concentrate by about 10 fold in tomato canning waste. There was found to be no concentration in processed or canned tomatoes. The DPR dietary analysis has six available tomato food form codes; tomatoes, whole, juice, puree, paste, catsup, and dried tomatoes (18, 19). Based on the reviewed data, the analysis allows to remain the 1.5 (juice) and 3.3 (puree) fold program's adjustment factor #1 for these tomato food forms. However, based on processing data the dietary program's adjustment factor #1 will be set to 1.0 (usual tomato paste is 5.4 and catsup is 2.5 fold) for the tomato food forms in both the acute and chronic sections. To account for the potential concentration of fenpropathrin in tomato waste, a 11.5 fold concentration based on the 0.13 ppm 3 day PHI residue value found on unwashed tomatoes in the T-7464 field study processing section will be used. This value (1.5 ppm) will be utilized and further explained in the secondary residues section. The assumption will be that all tomato waste residues found in animal feed will be a concentration of 1.5 ppm (11.5 fold concentration of .13 ppm RAC residue). This will account for potential residues that may concentrate in this product and potentially wind up in the feed of various domestic farm animals (24).

Secondary RAC Residues (beef...sheep)

Beef

The request for a California section 3 registration for cotton and the existing tomato section 18 will result in the potential of fenpropathrin residues to accumulate in the feed of various domestic farm animals. Animals fed a diet containing cottonseed products could result in residues in their tissues or produce (milk). The U.S. EPA maximum percentage contribution to cattle (beef and dairy) diet from cottonseed products is 25 percent (%) from seeds in the diet of beef cattle (24). The cotton product/cattle feed contribution range is 5-40%. The 40% contribution factor will not be used since it is for cotton forage and forage for animal feed is explicitly forbidden on the registrant label. The DPR assumption will be that 25% of all the feed of the various cattle will contain fenpropathrin residues at 3.0 ppm, the cottonseed oil feed additive tolerance.

Cattle also fed a diet containing tomato canning waste products could result in residues in their tissues or produce (milk). The U.S. EPA maximum percentage contribution to cattle (beef and dairy) diet from tomato canning waste products is 25 percent (%) from dry pomace in the diets of both beef and dairy cattle (24). The tomato canning waste product/cattle feed contribution range is 10-25%. The DPR assumption will be that 25% of all the feed of the various cattle will contain fenpropathrin residues at 1.5 ppm, the 11.5 fold concentration of the 0.13 ppm 3 day PHI RAC residue mentioned in the primary residue tomato section. This would mean that potentially 50% of the feed in the cattle diets could contain various amounts (assumption: 1.5 ppm in 25% and 25% at 3.0 ppm) of fenpropathrin.

The registrant has submitted a meat and milk feeding study and the fate of residues study in dairy cattle (5, 11). The data from these two studies will be used as surrogate residue data for goats, hogs, horses, and sheep tissues. The feeding study had three feed concentrations; 25, 75, and 250 ppm fenpropathrin. Measurable residues were found in the milk or meat samples of all three dose groups of 4 dairy cows each (11). The 25 and 75 ppm dose groups residues were to low to use for extrapolation to lower levels possible in the commercial cattle diet. The residue data indicates that fenpropathrin concentrates in animal fat and milk fat fractions. The 250 ppm residue data were extrapolated to approximate residues that might be found in 3.0 ppm and 1.5 ppm consumption diets of cattle.

The levels in cattle fed diets that had only cottonseed derived residues would have a maximum extrapolated acute value of 0.03 ppm in milk fat, 0.02 ppm in beef fat and 0.01 ppm (MDL) in all the other products (milk, various beef organs and meat). The acute milk fat value used is 0.03 ppm, the U.S. EPA tolerance, since no mixing in the cattle diet is assumed for short term duration feeding. The 0.02 ppm acute beef fat value is also the U.S. EPA tolerance based on the same assumption of no mixing of the cattle diet. All chronic beef/milk residue values were either 0.005 or 0.01 ppm except for milk fat and beef fat residues. The Non-fat milk components residues used 0.005 (1/2 MDL) based on the number of samples collected (N=44, range 0.002 - 0.006, AVG = 0.004 ppm) (11). The 0.013 ppm chronic milk fat value was derived by taking the 4.2 ppm (from 250 ppm diet) residue from the processed milk fraction section and dividing by 83.3 (adjustment to 3.0 ppm cottonseed oil tolerance from 250 ppm level) and then multiplying by 0.25 (25% maximum cottonseed contribution to cattle diet). The 0.012 ppm chronic beef fat value was derived by taking the 4.1 ppm (from 250 ppm diet) residue from the meat tissue section and dividing by 83.3 (adjustment to 3.0 ppm cottonseed oil tolerance from 250 ppm level) and then multiplying by 0.25 (25% maximum cottonseed contribution to cattle diet).

The levels in cattle fed diets that had only tomato canning waste derived residues would be calculated using the same methods as described in detail in the preceding paragraph. The maximum extrapolated acute values of 0.025 ppm in milk fat, 0.02 ppm in beef fat and 0.01 ppm (MDL) in all the other products (milk, various beef organs and meat) were used. The 0.02 ppm acute beef fat value, the U.S. EPA tolerance, is based on the extrapolation from 250 ppm and the assumption of no mixing of the cattle diet. The 0.025 ppm acute milk fat value was derived by taking the 4.2 ppm (250 ppm diet) residue from the processed milk fraction section and dividing by 167 (adjustment to 1.5 ppm tomato canning waste level from 250 ppm level). Since no mixing in the acute cattle diet is assumed, then the value is 0.025 ppm. All chronic beef and milk residues were 0.005, 0.006, or 0.01 ppm. The Non-fat milk component residues used 0.005 (1/2 MDL) based on the number of samples collected (N=44, range 0.002 - 0.006, AVG = 0.004 ppm) (11). The 0.006 ppm chronic milk fat value was derived by taking the 4.2 ppm (from 250 ppm diet) residue from the processed milk fraction section and dividing by 167 (adjustment to 1.5 ppm tomato canning waste level from 250 ppm level) and then multiplying by

0.25 (25% maximum tomato contribution to cattle diet). The 0.006 ppm chronic beef fat value was derived by taking the 4.1 ppm (from 250 ppm diet) residue from the processed tissue section and dividing by 167 (adjustment to 1.5 ppm from 250 ppm level) and then multiplying by 0.25 (25% maximum cottonseed contribution to cattle diet).

The potential level in cattle fed diets that had both cottonseed and tomato canning waste derived residues will be calculated using the same method described in detail in the previous paragraphs. The maximum combined contribution to cattle feed from fenpropathrin could be 50% based on 25% from cotton and 25% from tomatoes (24). The extrapolated acute values of 0.03 ppm in milk fat and 0.02 ppm in beef fat are both at their U.S. EPA tolerance levels. The other cattle products (milk, various beef organs and meat) acute values are 0.01 ppm (MDL). The 0.02 ppm acute beef fat and milk fat values are based on the extrapolation from 250 ppm concentrations and the assumption of no mixing of the acute cattle diet. The 0.019 ppm chronic milk fat value was derived by taking the 4.2 ppm (250 ppm diet) residue from the processed milk fraction section and dividing by 167 (adjustment to 1.5 ppm tomato level from 250 ppm diet) and multiplying by 0.25 (25% maximum tomato contribution). Then, the 4.2 ppm (250 ppm diet) residue is divided by 83.3 (adjustment to 3.0 ppm cotton level from 250 ppm diet) and multiplied by 0.25 (25% maximum cotton contribution). Finally the cotton and tomato portions are totaled (0.013 and 0.006 ppm respectively). The 0.019 ppm chronic beef fat value was derived by taking the 4.1 ppm (250 ppm diet) residue and adjusting the same as was done for the chronic milk fat. The cotton and tomato contributions are totaled (0.0125 and 0.006 ppm respectively) to arrive at 9 ppm beef fat extrapolated residue. All other chronic beef tissue (organs and meat) residues were 0.01 ppm. The Non-fat milk component residues used 0.005 (1/2 MDL) based on the number of samples collected.

Goats, Hogs, Horses, and Sheep Values

The red meat domestic farm animals included on the fenpropathrin U.S. EPA tolerances; goats, hogs, horses, and sheep will use the same residues, by meat tissue, as explained in the beef meat residue section. The beef residues and concentration from cotton, tomato, or cotton and tomato contributions to diet will be used as direct surrogates for these other red meat animals.

Poultry

Poultry fed a diet containing cottonseed products could result in residues in their tissues or eggs. The U.S. EPA maximum percentage contribution to poultry (chicken and turkey) diet from cottonseed products is 10 percent (%) in the diet of poultry (24). The cotton product/poultry feed contribution range is 3-10%. The 10% contribution factor will be used. The DPR assumption will be that 10% of all the feed of the various poultry will contain fenpropathrin residues at 3.0 ppm, the cottonseed oil feed additive tolerance (27).

A diet containing tomato canning waste products could also result in residues in poultry tissues or eggs. The U.S. EPA maximum percentage contribution to poultry (chicken and turkey) diet from tomato canning waste products is 3 percent (%) from dry pomace in the diets of poultry (24). The tomato canning waste product/poultry feed contribution range is 2-3%. The DPR assumption will be that 3% of all the feed of the various poultry will contain fenpropathrin residues at 1.5 ppm, the 11.5 fold concentration of the 0.13 ppm 3 day PHI RAC residue mentioned in the tomato primary residue section. This would mean that long term potentially 13% of the feed in the poultry diets could contain various amounts (assumption: 1.5 ppm in 3% and 10% at 3.0 ppm) of fenpropathrin.

The registrant has submitted a poultry (chicken) and egg feeding study plus a fate of the residue study in chickens (12, 15). The data from these two chicken studies will be used as surrogate tissue residue data for turkeys. The feeding study had three feed concentrations; 2.5, 7.5, and 25 ppm fenpropathrin. Measurable residues were found in the meat and egg samples of the 25 ppm dose group of 20 chickens (12). The 2.5 and 7.5 ppm dose groups residues were not detectable in the eggs or in any of the tissues except for fat. Therefore these two dose groups were to low to use for an extrapolation to levels possible in the commercial poultry diet. The residue data indicate that fenpropathrin concentrates in animal fat. The 25 ppm residue data were extrapolated to approximate residues that might be found in 3.0 ppm and 1.5 ppm residue consumption diets of poultry.

The levels in poultry fed diets that had only cottonseed derived residues would have a maximum extrapolated acute value of 0.02 ppm in poultry fat and 0.01 ppm (MDL) in all the other products (eggs and various poultry organs and meat). The acute poultry fat value used is 0.02 ppm, the U.S. EPA tolerance, since no mixing in the poultry diet is assumed for short term duration feeding. All chronic egg/meat residue values were either 0.005 or 0.01 ppm. The egg residue used 0.005 (1/2 MDL) based on the number of samples collected (N=12, range 0.001 - 0.002, AVG = 0.002 ppm) (15). The other residues were remained at 0.01 ppm even for chronic since only two samples were taken of each animal tissue.

Poultry fed diets that contained only tomato canning waste derived residues will be calculated using the same method as described in detail above. The maximum extrapolated acute value was 0.012 ppm in poultry meat fat. All the other products (eggs, various poultry organs and meat) were at 0.01 ppm (MDL). The 0.012 ppm acute poultry fat value is based on the extrapolation from 25 ppm feeding dose (adjusted to a 1.5 ppm consumption level in the poultry feed) and the assumption of no mixing of the short term diet derived residues. All chronic egg/meat residue values were either 0.005 or 0.01 ppm. The poultry extrapolated meat residues remained at 0.01 ppm even for the chronic dietary since only two samples were taken of each animal tissue. The egg residue used 0.005 (1/2 MDL) based on the number of samples collected (N=12, range 0.001 - 0.002, AVG = 0.002 ppm) (15).

The potential level in poultry fed diets that had both cottonseed and tomato canning waste derived residues will be calculated using the same method described in detail in the beef section combined cottonseed and tomato products dietary paragraphs. The combined maximum contribution to poultry feed from fenpropathrin could be 13% based on 10% from cotton and 3% from tomatoes (24). The extrapolated acute value of 0.02 ppm in poultry fat is the U.S. EPA tolerance level. The other poultry products (eggs, various organs and meat) acute values are 0.01 ppm (MDL). The 0.02 ppm acute poultry fat is based on the extrapolation from 25 ppm concentrations and the assumption of no mixing of the acute cattle diet. The chronic dietary assumes that the is mixing of the animal feed over time so that the average likely maximum residue contribution will be 13% for poultry. The 0.01 ppm chronic poultry fat value was derived by taking the 0.024 ppm extrapolated residue (adjustment to 3.0 ppm cotton level) and multiplied by 0.10 (10% maximum cotton contribution to the diet). The tomato (1.5 ppm tomato level) extrapolated value of 0.012 ppm was multiplied by 0.03 (3% maximum tomato contribution). The cotton and tomato contributions are totaled (0.0024 and 0.00036 ppm respectively) to arrive at 0.01 ppm (MDL). The actual extrapolated value was 0.003 ppm but the sample size was insufficient to use 0.005 ppm (1/2 MDL). All of the other chronic dietary residue values are set at either 0.005 ppm for eggs (1/2 MDL) or 0.01 ppm (MDL).

The submitted Valent, Inc. field and feeding studies data were the primary values used in the DPR dietary exposure assessment. The residue data not used in the dietary assessment were due to the USDA FSIS non-monitoring and the DPR, FDA, and USDA higher relative MDL/LQL levels as compared to the registrant's residue methods. Therefore, all presented RAC residue values used for Fenpropathrin were obtained from either Valent, Inc. registrant supplied field and feeding residue data or the appropriate U.S. EPA tolerance. Table 2 contains a summary of the relevant margin of safety data from conducting the acute and chronic dietary exposure assessments. A total of 22 raw agricultural and food/feed additive temporary tolerances were included in the DPR dietary analysis (25, 27).

APPENDIX C

Residue Data and Tolerance Asssessments

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRC01A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) - 6.0 mg/kg body-wt/day
COMMENT 1: Acute: Registrant field studies data
COMMENT 2: California cotton labeled use

RESIDUE FILE LISTING

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	#2	SOURCE[1] CODE
290	A	COTTONSEED-OIL	0.290000	3.00	1.00	REG-f
291	A	COTTONSEED-MEAL	0.290000	1.00	1.00	REG-f
318	X	MILK-NONFAT SOLIDS	0.010000	1.00	1.00	REG-fd
319	X	MILK-FAT SOLIDS	0.030000	1.00	1.00	EPA
320	X	MILK SUGAR (LACTOSE)	0.010000	1.00	1.00	REG-fd
321	U	BEEF-MEAT BYPRODUCTS	0.010000	1.00	1.00	REG-fd
322	U	BEEF(ORGAN MEATS)-OTHER	0.010000	1.00	1.00	REG-fd
323	U	BEEF-DRIED	0.010000	1.92	1.00	REG-fd
324	U	BEEF(BONELESS)-FAT	0.020000	1.00	1.00	EPA
325	U	BEEF(ORGAN MEATS)-KIDNEY	no consumption in survey			
326	U	BEEF(ORGAN MEATS)-LIVER	0.010000	1.00	1.00	REG-fd
327	U	BEEF(BONELESS)-LEAN (FAT/FREE)	0.010000	1.00	1.00	REG-fd
328	U	GOAT-MEAT BYPRODUCTS	no consumption in survey			
329	U	GOAT(ORGAN MEATS)-OTHER	0.010000	1.00	1.00	REG-fd
330	U	GOAT(BONELESS)-FAT	no consumption in survey			
331	U	GOAT(ORGAN MEATS)-KIDNEY	no consumption in survey			
332	U	GOAT(ORGAN MEATS)-LIVER	no consumption in survey			
333	U	GOAT(BONELESS)-LEAN (FAT/FREE)	no consumption in survey			
334	U	HORSE	no consumption in survey			
336	U	SHEEP-MEAT BYPRODUCTS	no consumption in survey			
337	U	SHEEP(ORGAN MEATS)-OTHER	no consumption in survey			
338	U	SHEEP(BONELESS)-FAT	0.020000	1.00	1.00	EPA
339	U	SHEEP(ORGAN MEATS)-KIDNEY	no consumption in survey			
340	U	SHEEP(ORGAN MEATS)-LIVER	no consumption in survey			
341	U	SHEEP(BONELESS)-LEAN (FAT FREE)	0.010000	1.00	1.00	REG-fd
342	U	PORK-MEAT BYPRODUCTS	0.010000	1.00	1.00	REG-fd
343	U	PORK(ORGAN MEATS)-OTHER	no consumption in survey			
344	U	PORK(BONELESS)-FAT	0.020000	1.00	1.00	EPA
345	U	PORK(ORGAN MEATS)-KIDNEY	no consumption in survey			
346	U	PORK(ORGAN MEATS)-LIVER	0.010000	1.00	1.00	REG-fd
347	U	PORK(BONELESS)-LEAN (FAT FREE)	0.010000	1.00	1.00	REG-fd
355	V	TURKEY-BYPRODUCTS	0.010000	1.00	1.00	REG-fd
356	V	TURKEY-GIBLETS (LIVER)	0.010000	1.00	1.00	REG-fd
357	V	TURKEY-(BONELESS)-FAT	0.020000	1.00	1.00	EPA
358	V	TURKEY-(BONELESS)LEAN/FAT FREE	0.010000	1.00	1.00	REG-fd
359	V	TURKEY-UNSPECIFIED	no consumption in survey			
360	V	POULTRY-OTHER-LEAN (FAT FREE)	0.010000	1.00	1.00	REG-fd

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) - 6.0 mg/kg body-wt/day

RESIDUE FILE LISTING (continued)

TAS CODE	CROP GRP	FOOD NAME	RESIDUE (PPM)	ADJ. FCTRS #1	ADJ. FCTRS #2	SOURCE[1] CODE
361	V	POULTRY-OTHER-GIBLETS(LIVER)	no consumption in survey			
362	V	POULTRY-OTHER-FAT	0.020000	1.00	1.00	EPA
363	X	EGGS-WHOLE	0.010000	1.00	1.00	REG-fd
364	X	EGGS-WHITE ONLY	0.010000	1.00	1.00	REG-fd
365	X	EGGS-YOLK ONLY	0.010000	1.00	1.00	REG-fd
366	V	CHICKEN-BYPRODUCTS	no consumption in survey			
367	V	CHICKEN-GIBLETS(LIVER)	0.010000	1.00	1.00	REG-fd
368	V	CHICKEN (BONELESS)-FAT	0.020000	1.00	1.00	EPA
369	V	CHICKEN(BONELESS)LEAN/FAT FREE	0.010000	1.00	1.00	REG-fd
385	V	CHICKEN-GIBLETS (EXCL. LIVER)	0.010000	1.00	1.00	REG-fd
398	X	MILK-BASED WATER	0.010000	1.00	1.00	REG-fd
424	U	VEAL-(BONELESS)-FAT	0.020000	1.00	1.00	EPA
425	U	VEAL-(BONELESS)-LEAN (FAT FREE)	0.010000	1.00	1.00	REG-fd
426	U	VEAL-(ORGAN MEATS)-KIDNEY	no consumption in survey			
427	U	VEAL-(ORGAN MEATS)-LIVER	no consumption in survey			
428	U	VEAL-(ORGAN MEATS)-OTHER	no consumption in survey			
429	U	VEAL-DRIED	no consumption in survey			
430	U	VEAL-MEAT BYPRODUCTS	no consumption in survey			
449	V	TURKEY-(ORGAN MEATS)-OTHER	0.010000	1.00	1.00	REG-fd

1/ EPA - U.S. EPA tolerance
REG-f - Registrant supplied field residue data
REG-fd - Registrant study - animal feeding data
REG-fp - Registrant study - field residue data with processing component

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRC01A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day
COMMENT 1: Acute: Registrant field studies data
COMMENT 2: California cotton registration
Initial estimate of user-days as % of person-days in survey = 100.00%

U.S. POP - ALL SEASONS

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.6%	0.000144	0.000154	0.000001	41713

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000031	191,952	20.0	0.000199	30,100
80.0	0.000047	127,699	10.0	0.000310	19,381
70.0	0.000062	97,060	5.0	0.000446	13,454
60.0	0.000078	76,738	2.5	0.000594	10,106
50.0	0.000097	61,929	1.0	0.000791	7,590
40.0	0.000119	50,498	0.5	0.000929	6,456
30.0	0.000149	40,155	0.0	0.003419	1,755

WESTERN REGION

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.6%	0.000149	0.000164	0.000002	40200

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000030	202,132	20.0	0.000214	27,982
80.0	0.000046	129,724	10.0	0.000313	19,193
70.0	0.000062	96,637	5.0	0.000439	13,673
60.0	0.000081	74,295	2.5	0.000591	10,144
50.0	0.000101	59,201	1.0	0.000849	7,064
40.0	0.000126	47,754	0.5	0.001047	5,730
30.0	0.000162	36,927	0.0	0.002386	2,515

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

HISPANICS

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.0%	0.000138	0.000148	0.000004	43363

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000027	219,942	20.0	0.000204	29,362
80.0	0.000040	150,191	10.0	0.000318	18,897
70.0	0.000052	116,398	5.0	0.000459	13,058
60.0	0.000065	91,829	2.5	0.000603	9,955
50.0	0.000088	68,000	1.0	0.000709	8,462
40.0	0.000111	53,914	0.5	0.000825	7,271
30.0	0.000145	41,264	0.0	0.001054	5,690

NON-HISPANIC WHITES

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.7%	0.000143	0.000152	0.000001	41816

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000033	181,419	20.0	0.000197	30,498
80.0	0.000049	122,547	10.0	0.000305	19,652
70.0	0.000064	94,382	5.0	0.000441	13,590
60.0	0.000080	75,388	2.5	0.000580	10,342
50.0	0.000098	61,343	1.0	0.000780	7,691
40.0	0.000119	50,395	0.5	0.000923	6,500
30.0	0.000149	40,275	0.0	0.003419	1,755

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

NON-HISPANIC BLACKS

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day)			
	Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.4%	0.000143	0.000166	0.000003	42062

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000024	252,569	20.0	0.000203	29,546
80.0	0.000036	167,103	10.0	0.000330	18,205
70.0	0.000051	118,059	5.0	0.000465	12,916
60.0	0.000069	87,489	2.5	0.000673	8,921
50.0	0.000091	66,231	1.0	0.000829	7,237
40.0	0.000115	52,246	0.5	0.000951	6,307
30.0	0.000145	41,408	0.0	0.001418	4,233

NON-HISPANIC OTHER

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day)			
	Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.9%	0.000164	0.000176	0.000006	36577

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000032	187,820	20.0	0.000246	24,391
80.0	0.000049	121,598	10.0	0.000337	17,814
70.0	0.000067	89,312	5.0	0.000453	13,251
60.0	0.000081	73,712	2.5	0.000657	9,128
50.0	0.000108	55,676	1.0	0.000917	6,542
40.0	0.000146	40,999	0.5	0.001099	5,460
30.0	0.000191	31,444	0.0	0.001736	3,455

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

NURSING INFANTS (<1 YEAR)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
82.6%	0.000097	0.000163	0.000022	61845

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000019	319,672	20.0	0.000124	48,549
80.0	0.000031	192,223	10.0	0.000170	35,308
70.0	0.000037	163,414	5.0	0.000278	21,591
60.0	0.000044	137,587	2.5	0.000581	10,332
50.0	0.000046	131,001	1.0	0.000791	7,589
40.0	0.000048	125,017	0.5	0.000861	6,972
30.0	0.000064	93,262	0.0	0.000931	6,447

NON-NURSING INFANTS (<1)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
90.2%	0.000292	0.000369	0.000021	20557

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000032	185,458	20.0	0.000484	12,405
80.0	0.000081	74,315	10.0	0.000779	7,706
70.0	0.000093	64,409	5.0	0.000986	6,083
60.0	0.000105	57,213	2.5	0.001213	4,947
50.0	0.000118	50,683	1.0	0.001764	3,401
40.0	0.000162	37,143	0.5	0.002115	2,837
30.0	0.000254	23,578	0.0	0.002386	2,515

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRC01A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

FEMALES (13+/PREG/NOT NSG)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day)			
	Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.6%	0.000110	0.000069	0.000004	54427

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000033	182,840	20.0	0.000158	37,907
80.0	0.000055	109,703	10.0	0.000208	28,897
70.0	0.000071	83,933	5.0	0.000245	24,490
60.0	0.000085	70,811	2.5	0.000271	22,109
50.0	0.000098	61,348	1.0	0.000334	17,954
40.0	0.000114	52,653	0.5	0.000355	16,883
30.0	0.000132	45,606	0.0	0.000461	13,022

FEMALES (13+/NURSING)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day)			
	Mean	Standard Deviation	Standard Error	Margin of Safety 1/
100.0%	0.000124	0.000091	0.000007	48550

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000037	163,225	20.0	0.000187	32,061
80.0	0.000049	123,215	10.0	0.000248	24,210
70.0	0.000062	96,508	5.0	0.000335	17,909
60.0	0.000084	71,613	2.5	0.000370	16,208
50.0	0.000095	63,361	1.0	0.000430	13,961
40.0	0.000114	52,581	0.5	0.000474	12,651
30.0	0.000152	39,501	0.0	0.000509	11,788

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRC01A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

CHILDREN (1-6 YEARS)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.9%	0.000416	0.000249	0.000005	14411

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000155	38,820	20.0	0.000603	9,949
80.0	0.000215	27,868	10.0	0.000745	8,055
70.0	0.000262	22,871	5.0	0.000875	6,856
60.0	0.000311	19,266	2.5	0.001015	5,910
50.0	0.000367	16,367	1.0	0.001275	4,705
40.0	0.000428	14,009	0.5	0.001375	4,363
30.0	0.000498	12,054	0.0	0.001736	3,455

CHILDREN (7-12 YEARS)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
100.0%	0.000260	0.000160	0.000003	23091

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000088	67,848	20.0	0.000374	16,037
80.0	0.000127	47,144	10.0	0.000481	12,482
70.0	0.000164	36,649	5.0	0.000562	10,669
60.0	0.000195	30,819	2.5	0.000657	9,136
50.0	0.000228	26,263	1.0	0.000842	7,128
40.0	0.000264	22,703	0.5	0.000926	6,482
30.0	0.000311	19,304	0.0	0.001081	5,548

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRC01A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) - 6.0 mg/kg body-wt/day

MALES (13-19 YEARS)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
100.0%	0.000156	0.000094	0.000003	38510

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000054	111,940	20.0	0.000233	25,737
80.0	0.000073	81,686	10.0	0.000288	20,851
70.0	0.000093	64,178	5.0	0.000334	17,972
60.0	0.000115	52,241	2.5	0.000391	15,356
50.0	0.000136	44,159	1.0	0.000448	13,400
40.0	0.000166	36,196	0.5	0.000466	12,878
30.0	0.000194	30,970	0.0	0.000668	8,985

FEMALES (13-19 YRS/NP/NN)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
100.0%	0.000132	0.000116	0.000003	45577

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000037	164,112	20.0	0.000189	31,665
80.0	0.000054	110,818	10.0	0.000233	25,771
70.0	0.000075	79,801	5.0	0.000314	19,131
60.0	0.000093	64,303	2.5	0.000376	15,972
50.0	0.000112	53,433	1.0	0.000486	12,353
40.0	0.000136	43,999	0.5	0.000532	11,274
30.0	0.000160	37,389	0.0	0.003419	1,755

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

MALES (20+ YEARS)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.6%	0.000097	0.000071	0.000001	61893

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000030	197,752	20.0	0.000139	43,119
80.0	0.000044	137,269	10.0	0.000179	33,461
70.0	0.000055	108,533	5.0	0.000227	26,437
60.0	0.000068	88,571	2.5	0.000271	22,116
50.0	0.000081	73,687	1.0	0.000325	18,459
40.0	0.000097	61,850	0.5	0.000390	15,403
30.0	0.000116	51,838	0.0	0.001271	4,720

FEMALES (20+ YEARS/NP/NN)

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.7%	0.000086	0.000061	0.000001	69937

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE
(in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000024	247,081	20.0	0.000125	47,885
80.0	0.000037	163,985	10.0	0.000165	36,433
70.0	0.000048	124,195	5.0	0.000204	29,342
60.0	0.000060	99,550	2.5	0.000244	24,605
50.0	0.000072	83,790	1.0	0.000296	20,283
40.0	0.000086	69,500	0.5	0.000352	17,031
30.0	0.000104	57,815	0.0	0.000829	7,241

ACUTE EXPOSURE (EX4) ANALYSIS FOR FENPROPATHRIN; Section 3 Registration
Residue file name: FNPRCO1A (NFCS87/88 DATA) Analysis date: 05-23-1994
DPR NOEL (Acute) = 6.0 mg/kg body-wt/day

CUSTOM DEMOGRAPHICS 1: Seniors 55+ Years

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.9%	0.000091	0.000070	0.000001	66247

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE (in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000028	216,437	20.0	0.000128	46,747
80.0	0.000040	148,838	10.0	0.000166	36,121
70.0	0.000052	114,313	5.0	0.000213	28,220
60.0	0.000064	94,072	2.5	0.000260	23,103
50.0	0.000075	79,587	1.0	0.000321	18,714
40.0	0.000090	66,421	0.5	0.000369	16,255
30.0	0.000107	55,977	0.0	0.001271	4,720

CUSTOM DEMOGRAPHICS 2: U.S. Population, 16+ Years

ESTIMATED PERCENT OF PERSON-DAYS THAT ARE USER-DAYS	MEAN DAILY EXPOSURE PER USER-DAY (mg/kg body wt/day) Mean	Standard Deviation	Standard Error	Margin of Safety 1/
99.7%	0.000095	0.000070	0.000000	63318

ESTIMATED PERCENTILE OF POPULATION USER-DAYS EXCEEDING CALCULATED EXPOSURE (in mg/kg body wt/day)

PERCENTILE	EXPOSURE	MOS	PERCENTILE	EXPOSURE	MOS
90.0	0.000028	216,170	20.0	0.000138	43,519
80.0	0.000041	146,385	10.0	0.000179	33,524
70.0	0.000053	112,979	5.0	0.000225	26,681
60.0	0.000065	92,097	2.5	0.000269	22,344
50.0	0.000079	75,979	1.0	0.000337	17,802
40.0	0.000095	63,318	0.5	0.000394	15,210
30.0	0.000113	53,231	0.0	0.001271	4,720

1/ Margin of Safety = NOEL ÷ Dietary Exposure